The New England
Journal of Medicine

Copyright, 1945, by the Massachusetts Medical Society

Volume 232 MARCH 8, 1945 Number 10

EPOCHS IN THE HISTORY OF THE WORCESTER DISTRICT MEDICAL SOCIETY*

ROY J. WARD, M.D.

WORCESTER, MASSACHUSETTS

WE ARE now living in an age of science. Of all the sciences none have affected the welfare and happiness of the ordinary man more than has the science of medicine.

At the time of the founding of the Worcester District Medical Society, whose one hundred and fiftieth birthday is being celebrated tonight, medicine was just beginning to feel its growing pains. For years, prior to 1794, periodic epidemics of smallpox, diphtheria, typhoid fever, cholera and yellow fever had swept over Europe and America, threatening the lives of everyone. Today, we no longer wilt before the ravages of such epidemics. We have learned to control pain, wound infection, hemorrhage and shock. Tuberculosis and pernicious anemia, which were always fatal, are now responding to treatment. It is my purpose to give a picture of this district in 1794, and to trace the part that the physicians of this community played in this remarkable achievement of medical science.

In preparation, I have reviewed historical papers from the pens of Drs. Samuel B. Woodward, Homer Gage, Lemuel F. Woodward, Albert C. Getchell, Lester C. Miller and Albert M. Shattuck. Dr. Thomas H. Gage wrote the first historical sketch in 1854, but intense search for it has failed to locate any copy. I am also indebted for the splendid help that I have received from the staff of the American Antiquarian Society and its director, Mr. Clarence D. Brigham. Dr. William F. Lynch, chairman of the Anniversary Committee, and Dr. John Fallon, the librarian, have aided in collecting material and have been generous in constructive criticism; both have been an inspiration.

On December 18, 1794, forty-one physicians assembled at the United States Arms Hotel to form the Worcester Medical Society. Thirty-six of them rode into Worcester on horseback. They came from as far west as the Connecticut River and as far east as Mendon. Only one of them, Dr. John Frink, of Rutland, was a member of the Massachusetts Medical Society, and only one ever had attended a medical lecture or a medical school. They came as a protest against the Massachusetts Medical Society, which had limited its membership to seventy and in thirteen years had elected to membership only one man from west of Framingham.

Worcester, a town of 2000 inhabitants, was selected as the meeting place, not because of its size, — for Charlton and Sutton were larger, — but because it was on the stage route between Boston and New York, and because the United States Arms Hotel was the best hotel in the county. Except for the stage route, roads were very poor. Many were mere bridle paths. Only the wealthy owned a wheeled vehicle or chaise; hence, everyone walked or rode horseback.

The early records tell little about the medical problems discussed at the meetings of those days. It is known that they took the form of case reports, which today constitute a favorite method of presenting medical subjects. It is also known that Worcester County at that time was in the throes of an epidemic of smallpox, meningitis and dysentery, and that smallpox alone killed 4 per cent of the population.

The study of medicine at the time of the founding of this society was almost entirely by the preceptor system. Harvard Medical School had been in operation for twelve years, but by 1793 had graduated only ten students,† so that the preceptor system was the only one available to the majority of students. Dr. Samuel B. Woodward in his oration before this society in May, 1898, gave an interesting story of the mechanics of that system that is worth quoting in its entirety.

> Each . . . [student] had studied with a preceptor, a plan not yet entirely given up as a part of a medical education, and at that time the only plan practicable.
>
> A cynical description alleges that studying with a country doctor in 1790 meant chiefly "the care of the doctor's horse, doing chores about the house, assisting the instructor in gathering and drying the herbs and simples, preparing the powders and the pills and, on rare occasions, helping in some minor surgical operation."

*Read in part at the one hundred and fiftieth anniversary of the Worcester District Medical Society, Worcester, May 10, 1944.

†By the act of Legislature incorporating the Massachusetts Medical Society in 1781 the Society was empowered to examine applicants for license to practice medicine in the Commonwealth. Harvard Medical School was given the same right for its graduates.

An indenture of 1760, quoted by Norwood, sheds such light upon the position of the apprentice, showing that the student's relations with his instructor were not in truth always and entirely one sided.

> . . . during all which Term [four years and six months] the said Apprentice his said Master well and faithfully shall serve, his secrets keep, his lawful commands everywhere obey. He shall do no damage to his said Master, nor see it to be done by others, without letting or giving notice to his said Master. He shall not contract matrimony within said term. At cards, dice, or any other unlawful game he shall not play, whereby his said Master may have Damage. He shall not absent himself day or night from his said Master's Service without his leave, nor hant Ale houses, Taverns, or playhouses, but in all things, as a faithful Apprentice he shall behave himself toward his Master all during his said term. And the said Master, during the s'd term, shall by the best of his Means or Methods, Art and Mysterys of a Physician and Surgeon, as he now Professes Teach or cause the said Apprentice to be taught to perfection in consideration of the sum of One Hundred Pounds Lawful money of New York to him in hand paid. . . .
>
> And the said William Clark acknowledges himself herewith contented and the Receipt thereof. And the said Master is to provide his said Apprentice with sufficient Meat, Drink, Washing and Lodging and Mending his said clothes, within the said term, and the said James Hubbard is to find him in wearing apparel during said term aforesaid. . . . At the end of Said term the Said Master shall and will give unto the Apprentice a new set of surgeons pocket instruments, Solomon's Dispensatory, Quences' Dispensatory, and Fuller on Fevers, and for the true performance of all and every of the said covenants: . . . .

It was also customary to furnish the embryonic doctor with a certificate setting forth . . . "Mr. John Smith hath served as an apprentice to me for nearly four years, during which time he was constantly employed in the practice of Physics and Surgery, under my care, in which character he always behaved with great fidelity and industry. . . ."

Fortified with a like testimonial each man did set himself to work.

Dr. Austin Flint, of Leicester, was conducting a hospital in Worcester County for the inoculation of smallpox, and later was the first physician in the district to use the new method of vaccination with cowpox. Such subjects as these must have been uppermost in the members' minds and have made up the discussions of these early meetings. They were also looking into the future, for one of the most important actions of the newly formed society was to raise the educational requirements for the study of medicine, demanding a knowledge of Latin, Greek, elementary mathematics, natural history and natural philosophy.* This was just ninety years before Harvard Medical School required as much.

In 1798 the problem came up of providing for a library, and Dr. Elijah Dix, an active physician, an apothecary and an extensive real estate dealer, offered to give 50 pounds to the society for the purchase of books. This offer was accepted and a librarian was duly elected. Thus our library dates from this offer made in 1798, although Dr. Dix failed to keep his promise to provide the money for purchasing the books.

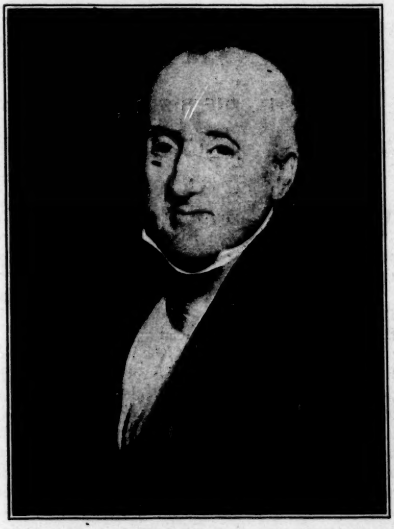

FIGURE 1. *Daniel Waldo.*

In 1804, after ten years' struggle with the Massachusetts Medical Society, that society's charter was so modified as to admit any respectable member of the profession. It also provided for district societies, and the Worcester Medical Society was the first one to join as a body.

In 1823, a campaign was started to raise a fund for more books for the library, and a generous subscription was received from Mr. Daniel Waldo (Fig. 1), a well-to-do merchant and importer owning

*Article 17 of the Laws and Regulations of Worcester Medical Society, adopted January 20, 1795, reads as follows:

"In order that the education of pupils should be more uniform and reputable it is the sense of this organization that before a person be qualified to enter upon the study of physick it is necessary that he have not only an accurate knowledge of his native tongue, but so much of the Latin and Greek as to translate them by the help of a dictionary, together with a knowledge of at least the elementary parts of mathematics, of natural history and of natural philosophy. . . . Before any pupil offer himself for examination, the physician who recommends him shall be certain that he has such a knowledge of anatomy as is necessary to understand the animal economy, its sound and morbid state, likewise an acquaintance with disease and the usual method of treating them, also a knowledge of the principles of chemistry, materia medica and the operation of medicine. As the art of physick is a mystery concerning which those who are not medically educated have not the means of judging so as readily to distinguish between the real physician and the imposing pretender, it appears highly reasonable that some criterion should be established by which those who are qualified for practice may be known, and in order, therefore, to prevent impositions whose consequences may prove so fatal and to assist mankind in forming a judgment in a matter to them so important, this Association declares it as their decided opinion that no physician ought to be encouraged in his profession unless he has passed an examination before some regularly appointed judges. The advantage of teaching physick by lectures is confessed by the usage of all Europe but has never been enjoyed among us until within a few years. We being persuaded that great advantage will result from such systematic mode of teaching all the branches of the medical art do hereby recommend to all such as are or may become our pupils to attend the medical lectures which are annually given at the University of Cambridge."

stores in Worcester and Boston. This was supplemented by a loan of fifty books from the Boston Medical Library. From then on the fortunes of this society rose and fell with the interest shown in the library. The records show that the library was moved from place to place because of the lack of a permanent home. When dust gathered on the books and they were scattered through the houses of the members, interest in the society also waned.

In 1845, Mr. Daniel Waldo left by will, among other benefactions, including a gift to the Massachusetts General Hospital, $5000 to this society "for the purchase of costly but useful inventions for surgical purposes, and for books treating on medical subjects . . . to the end that the science of medicine . . . may be more fully understood and the community benefited by able and enlightened physicians and surgeons." The books purchased from this fund increased the problem of a suitable place to house them. Dr. John Green offered a room, free of rent for a year, over his apothecary shop on Main Street. This is the same Dr. Green who left the bulk of his fortune to found the Worcester Public Library. He evidently had his peculiarities, as illustrated by a sketch of him driving down Main Street (Fig. 2). His bookplate (Fig. 3) shows that he covered the whole medical field. It is also recorded that he, with a Dr. Benjamin Heywood, sought to monopolize the practice of medicine in Worcester by refusing to consult with any new physician who came to town. Dr. Samuel B. Woodward is authority for the story that Dr. Homans, father of Dr. John Homans, of Boston, was one of these, and that Dr. Joseph Sargent was the first physician who succeeded in breaking down this monopoly.

At the opening of the Free Public Library in 1861 the books of the society were moved to comfortable rooms on the first floor, where there were ample bookshelves and room to hold the meetings. It was during this time that the library was considered the peer of any medical library in the country. It was in this location that the society flourished until 1899, when, owing to overcrowding, the books were moved to the attic. This was unfortunate. The space under the mansard roof was dingy, dirty and accessible only by a one-man elevator. There was not room enough for medical meetings, and the library pined.

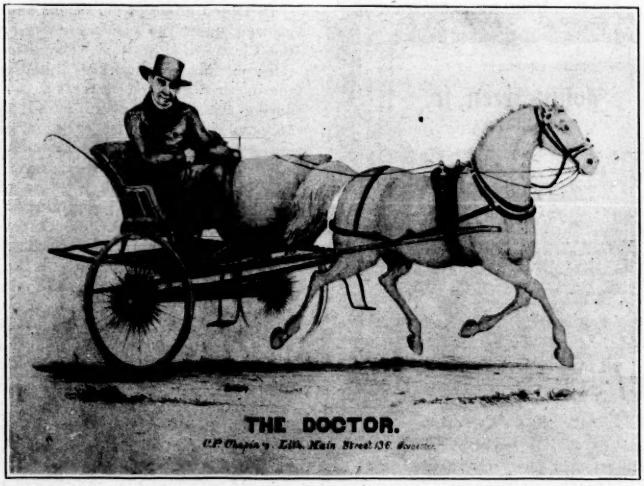

FIGURE 2. *A Characteristic Pose of Dr. John Green.*

In 1933, the library was again asked to move. Under the leadership of the Library Committee, consisting of Drs. A. W. Marsh, Ernest L. Hunt and John Fallon, a new home was found at 34 Elm Street. This energetic committee fitted up the reading room attractively, but owing to lack of money most of the books were left lying in bundles in the basement. As a part of the renaissance of the library a new corporation was formed, the Worcester Medical Library, Incorporated, embracing all members of the society.

In 1904, Dr. Homer Gage, in his annual oration,

suggested a building to house the library and all the society activities, and he frequently suggested a site for such a building, but the time was not ripe. In 1935 he again made the same suggestion. Even

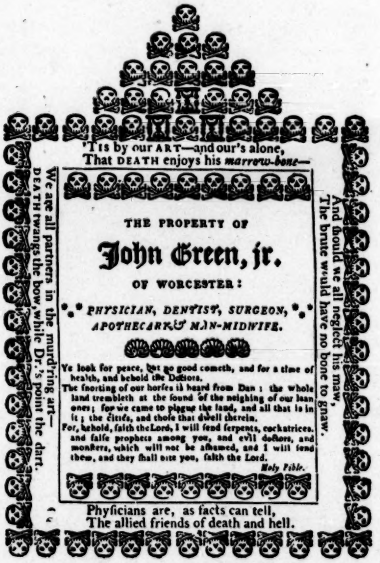
'Tis by our ART—and our's alone,
That DEATH enjoys his marrow-bone—
We are all partners in the murdering art—
DEATH twangs the bow, while Dr.'s point the dart.
THE PROPERTY OF
John Green, jr.
OF WORCESTER:
PHYSICIAN, DENTIST, SURGEON,
APOTHECARY & MAN-MIDWIFE.
Ye look for peace, but no good cometh, and for a time of health, and behold the Debtors.
The snorting of our horses is heard from Dan: the whole land trembleth at the sound of the neighing of our lean ones; for we came to plague the land, and all that is in it; the cities, and those that dwell therein.
For, behold, saith the Lord, I will send serpents, cockatrices, and false prophets among you, and evil doctors, and monsters, which will not be affrayed, and I will send them, and they shall bite you, saith the Lord.
Holy Bible.
And should we all neglect his trade,
The brute would have no bone to gnaw.
Physicians are, as facts can tell,
The allied friends of death and hell.

FIGURE 3. *Dr. Green's Bookplate.*

when the library was adequately housed at 34 Elm Street only half the members paid their dues. It was a battle to keep the rent paid, and only the most valuable of the magazines were bound. An $18,000 appropriation was secured through the Works Progress Administration and the books were recatalogued and new stacks built, but finances continued to be a constant worry to the trustees. At their instigation a committee was appointed that, under the able leadership of Dr. Joel Melick, arranged a benefit lecture by Mrs. Franklin D. Roosevelt on "Peace." This was a financial success and was followed by three other benefits. These might have been continued had not the war intervened. More than $6000 has been raised by this method, most of which has been put away for a building fund.

With the advent of the present war the problem of financing the activities of the society and the library increased. One third of the members had entered the armed forces. An unprecedented budget was brought in, large enough to cover not only the old but also some new activities. This was presented with trepidation, but the members themselves raised it still higher to provide a yearly nest egg. Thus, the members at home have pledged themselves to carry the financial burden for their comrades in arms.

In 1942 the library again moved. The trustees were in a dilemma. They searched the city for an available place. Many sites were found and abandoned because of expense. Then the Blood Bank Committee came forward with a proposition that the library share a small part of their building (Fig. 4), and sold to it one seventh of their building, in which it is now located, in crowded but useful quarters.

In 1906 a group of physicians and lay people organized, under the auspices of the Fresh Air Fund, the Clean Milk Stations Committee. Since mortality records were first kept it had been noted that the death rate among infants was extremely high during the summer months, and physicians were accustomed to postpone their vacations until the fall in order to care for the large number of gastrointestinal cases that were the cause of this mortality. The success of this initial effort to combat the disease was so obvious that the society voted to organize the Medical Milk Commission, to encourage the production of certified milk. This commission still is functioning and has been a large factor in saving hundreds of children's lives.

In 1936, this society blazed a new trail. Inspired by Dr. Arthur M. Kimberly, the *Worcester Medical News*, now under the guiding hand of Dr. Francis J. Steele, was started. It was the first modern district-society journal in Massachusetts and is now demonstrating its worth every month. Ninety years ago the Worcester Medical College published a medical journal extolling the virtues of the Thomsonian system of medicine (Fig. 5).

It has been said that the modern hospital is the greatest clinical laboratory that society possesses, and that to it is owed most of the advances in medicine that have taken place. The Worcester District has not lacked in this respect. It has the first hospital ever built by tax funds for the care of the insane. This hospital was constructed by the State in 1832 on land provided by the city on Summer Street. Its first superintendent, Dr. Samuel B. Woodward, was the ancestor of the famous Woodward medical family, of whom the present Dr. Samuel B. Woodward survives. The latter is the authority for the following story of the opening of the hospital. Patients were admitted from all over the State — some from almshouses, jails and dungeons, where they had been kept under restraint. One man was brought chained inside of a wooden cage on a cart. When the new superintendent ordered the attendants to open the cage and unchain him, they remonstrated, but instead of attacking them, the patient knelt and raised his hands to worship Dr. Woodward, thinking that he must be God.

In 1864, the United States Army opened the Dale General Hospital (Fig. 6) on Union Hill, occupying part of the buildings formerly used by the Worcester Medical College. Built to accommodate 1000 beds and with fourteen one-story wards, it was never filled. It was later abandoned after a vain attempt was made by the Federal government to have the city or state take it over. In 1867, Reverend John J. Powers opened a small hospital that was operated by the Sisters of St. Anne's Convent — interestingly enough, for poor patients who prepaid a small amount each year.

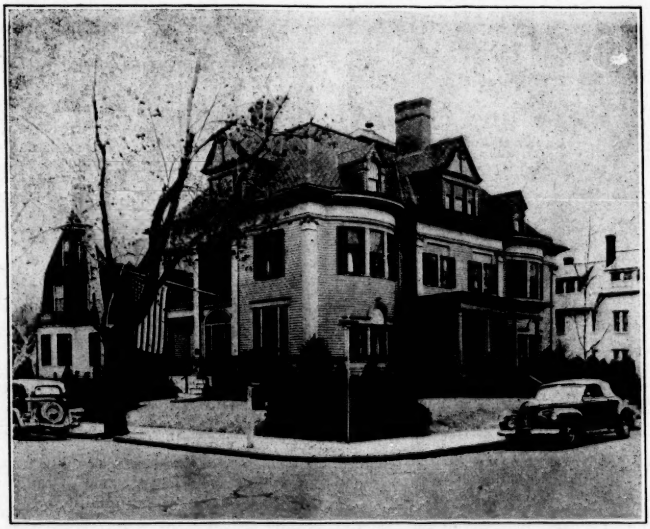

FIGURE 4. *Home of the Worcester Medical Library, Incorporated, and the Blood Bank.*

In 1871, on the recommendation of Dr. Albert Wood, Worcester established the City Hospital at Front and Church streets, in the Abigail Bigelow House, with accommodations for eight or ten patients. Dr. Leonard Wheeler was the first superintendent and insisted on clinical records being kept, much to the displeasure of his visiting staff.

One of the first community hospitals to be started in the surrounding towns was at Clinton. In 1888, the Clinton Hospital Association opened its doors in a rented tenement for the admittance of its first patient, who promptly died. Discouraged but not disheartened, the association grew by dint of hard work, and now has an up-to-date hospital of seventy-four beds. Dr. Walter P. Bowers has been the president of the corporation for fifty years. Although there is some debate regarding where the first hysterectomy in the district was performed, Dr. Peabody, former superintendent of the Worcester City Hospital, is the authority for the statement that it was done in the Clinton Hospital.

To Dr. Frank Washburn must be given the credit for establishing the Holden Cottage Hospital, a model of its kind and already so useful in its community that it is taxed beyond capacity.

Time does not permit enumerating the seventeen hospitals that have been established in this district since that early beginning on Front Street. Since then a magnificent system of hospitals has grown up all over the district, in large and small towns as well as in the city. Of the 6629 beds now available nearly half are outside the city limits. The rapid spread of community hospitals has added a great deal to the comfort and safety of the countryside.

The onset of the present war and the increasing use of blood for transfusions demonstrated the need of a supply for this district. At the January, 1942, meeting of the society, the pathologists of the city, Drs. Raymond Goodale, James Beck, William Moran and William Freeman, suggested the appointment of a committee to establish a blood bank. Headed first by Dr. Walter C. Seelye, and later by Dr. Edwin R. Leib, as president and Dr. William Freeman as secretary and director of the laboratory, the committee purchased a building, reconstructed it, installed equipment and has processed blood from 5000 donors. Both whole blood and blood plasma

are now distributed through twenty-four stations throughout southern Worcester County. The Cushing General Hospital at Framingham and the Lovell General Hospital at Fort Devens are

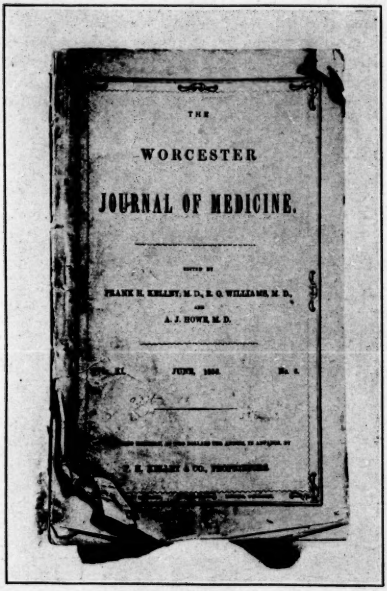

FIGURE 5. *The Cover of an Issue of the* Worcester Journal of Medicine.

also supplied. This outstanding voluntary effort on the part of the committee has been ably seconded by a splendid group of lay workers and donors, without whose aid it would have been difficult to carry on.

In 1869, the State Board of Health, the first of its kind, was established at Boston. Nine years later a city board was established in Worcester, with Dr. Rufus Woodward as the first secretary and executive officer. Since then, under the leadership of the medical profession, it has steadily increased its usefulness. One of our members, the late Dr. Thomas Kenney, was instrumental in reorganizing the setup. He built a $1,000,000 addition to the Putnam Division of Belmont Hospital and pushed through, against considerable opposition, a plan for immunization of the school population against diphtheria, which has saved thousands of lives.

In 1894, the Health Department established a laboratory for the examination of sputums for tubercle bacilli and cultures for diphtheria bacilli. This was the first municipal laboratory in New England and one of the first in the country after that begun in New York City. It was the beginning of a concerted attack on these two diseases in the district, which has led to remarkable results. A statistical study made some time ago revealed the fact that this city has been made the richer by $10,000,000* over and above the cost of the department during the last twenty years because of the prevention of sickness and the saving of lives.

During the earliest days the Worcester District Medical Society met alternately in Rutland and Worcester. Later most of the meetings were held in various halls and clubrooms about the city, except in the period 1861–1899, when the meetings were held in the Worcester Public Library. It was often recorded that after the morning session the society adjourned for dinner at the American Temperance House on Foster Street (Fig. 7). For several years the society met occasionally at various hospitals, but a great stride forward was taken in 1923 when, during Dr. A. W. Marsh's presidency, the meetings were transferred to the hospitals in the district. This was a great boon to both interest and attendance.

With the multiplication of activities by the society the officers have come to lean more and more on the assistant to the librarian, first Mrs. Barbara McPherson and now Mrs. Marjorie Edwards. In addition to her duties in the Worcester Medical Library, the assistant is a great help to the secretary, the treasurer and the editor and business manager of the *Worcester Medical News*. Her services have been increasingly valuable to the whole society.

No history of the society would be complete without at least mention of some of the controversies that took place. Opposition to homeopathy and eclectic medicine raged in Worcester as it had all over the country for twenty-five years, from 1852 to 1877. Many men were expelled from the society for practicing these systems or consulting with their practitioners.

In 1845, Dr. Calvin Newton, a graduate of Berkshire Medical College, erected on Union Hill a large building where he established his Botanico-Medical College. This building, later part of the Dale General Hospital and now Davis Hall at Worcester Academy, was built by funds subscribed by friends of the eclectic or Thomsonian system of medicine. The name of the school was changed from time to time, finally ending as Worcester Medical College. It received a charter from the Legislature in spite of strong opposition from the Massachusetts Medical Society, and for a while had a large group of students. There were six physicians and scientists on

*This study was made by me in conjunction with a paper read at a meeting of the Worcester District Medical Society in September, 1940. The figures were studied by Dr. H. L. Lombard, of the State Department of Public Health, who said: "Your figures are too low. . . . This goes to show that public-health work pays dividends."

its faculty who gave courses of lectures of fourteen weeks, beginning each March. The tuition was $50, with an additional fee of $25 for an elaborate diploma. Dr. Newton died in 1853, and with him collapsed his college and its medical magazine. The Middlesex University College of Medicine now operates under this charter. Dr. Newton, at one time a member of the Worcester District Medical Society, was expelled for violation of its bylaws.

In Hersey's *History of Worcester*, published in 1862, there were listed twenty-six allopathic, four eclectic, four homeopathic, one Thomsonian and four female physicians. In 1904 Dr. Homer Gage, in his oration before the society, quoted Dr. William Osler as stating:

> There are two factors in the progress of medicine, one the skeptical spirit fostered by Paris, Vienna and Boston physicians and second, and above all, the valuable lessons of homeopathy, the infinitesimals of which certainly would do no harm and quite as certainly do no good. A new school of practitioners has arisen which cares nothing for homeopathy and less for so called allopathy. It seeks to study rationally and scientifically the action of drugs, old and new.

Thus has passed into history a controversy that was vigorous while it lasted. I prophesy that at some time whatever is of merit in any of the methods of therapy not now approved by the society will eventually be accepted by the medical profession.

Worcester District Medical Society has furnished the Massachusetts Medical Society with five of its presidents. The first of these was Dr. Thomas H. Gage (1886–1888), father of the late Dr. Homer Gage. He was the author of many medical papers, one of which on typhoid fever was epoch-making. He was a prominent churchman, was on the staff of the Worcester City Hospital, and was active in civic affairs. He was for years a member of an important committee of the parent society, the Committee on Ethics and Discipline. The second was Dr. Edwin B. Harvey (1898–1900), of Westboro. He was a member of the Legislature, and during that time he was the author of the law establishing the Board of Registration in Medicine and was for many years secretary of that board. The third was Dr. George B. Francis (1902–1904), of Worcester, a Civil War surgeon. It was his steadfast demand that opened the doors of the Massachusetts Medical Society to women. The fourth was Dr. Walter P. Bowers (1912–1914) of Clinton, at one time secretary of the State Board of Registration in Medicine. When the *Boston Medical and Surgical Journal* was taken over by the Massachusetts Medical Society, Dr. Bowers was the first editor-in-chief. No words can express the debt that the whole profession owes to him for the magnificent job that he did. The fifth was Dr. Samuel B. Woodward (1916–1919). He is a surgeon, the author of many surgical papers and a historian *par excellence*.

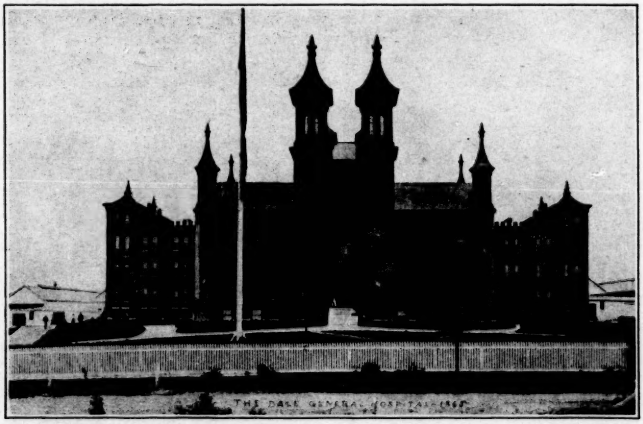

FIGURE 6. *The Dale General Hospital.*

The opportunity must not be missed of reminding the society of the debt that it owes those who have furthered its aspirations for a "better city and a more enlightened profession," as Daniel Waldo wrote in his will.

Mr. Waldo was the first of these. Born in Boston, he came to Worcester at the age of nineteen, lived in his father's home at Lincoln Square and died in his stately residence on Main Street, at the present site of Mechanics Hall. He was a churchman, merchant, successful business man, importer and philanthropist. Mr. Harrison Bliss (Fig. 8), another benefactor, was at one time coachman for Dr.

Oliver Fisk, the first secretary of the society. He was a merchant, railroad president, city alderman and representative in the General Court.

Dr. Charles Wilder (Fig. 9), of Leominster, at one time president of the society, fathered a movement to build a county hospital in Worcester. Dr. Leonard Wheeler, first superintendent of the Worcester City Hospital, a gynecologist and president of the Board of Trustees of Memorial Hospital, wrote a famous paper on the Waldo, Wilder and Bliss Fund. He spent many hours on the problems of the Worcester Medical Library. Dr. Donald Delahanty, a former president and a councilor for many years, was noted for his sympathy for the underdog. No one ever called on him in vain for help.

Dr. Samuel B. Woodward is one of the few members who have occupied all the offices in the gift of the society, having served as secretary, treasurer, president and councilor, as well as president of the Massachusetts Medical Society. He has been noted for his interest in the welfare of the city, and for years was president of the Worcester County Institution for Savings, the Taxpayers

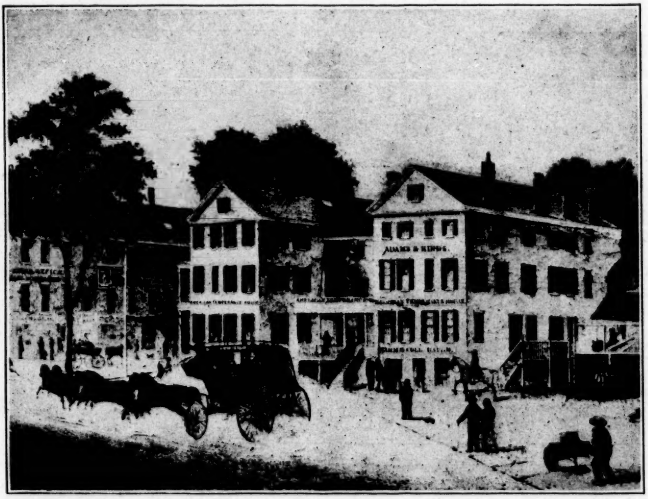

FIGURE 7. *The American Temperance House.*

Adams, a captain in the United States Army in World War I, a surgeon at the Memorial Hospital, died in the flower of his work. To Dr. Edgar A. Fisher, a retiring man with unusual surgical and organizing ability, the success of the Hahnemann Hospital is in a considerable measure due. Dr. Michael Fallon, former president of the society, was a member of the State Board of Registration in Medicine, a councilor of the Massachusetts Medical Society for many years and the author of innumerable papers on surgery. He was for many years surgeon-in-chief and president of the staff of St. Vincent Hospital, and was an outstanding Catholic layman. Dr. Homer Gage, a former president of the society, famous son of a famous father, was successful in business as well as in surgery, a rare combination. He had plans for the future of the society that have never matured. These plans, made in 1904, are our goal today. Dr. William Association and the Society for the Prevention of Cruelty to Children.

In Worcester County a pioneer work in industrial medicine has been done. Dr. W. Irving Clark, since 1911 head of the medical service at the Norton Company, and Dr. Theodore L. Story, since 1925 medical director of the American Optical Company, have blazed new trails in the care of thousands of industrial employees. Finally, Dr. James C. McCann, president of the Blue Shield, was largely responsible for the creation of that organization.

There are many more interesting epochs a satisfactory reporting of which space does not permit. Chief among these is the story of the contribution that this district has made to the war effort, from 1812 down to the present time.

Santayana has written, "He who does not remember history has to repeat it." It is hoped that by refreshing our minds from time to time concerning the past we can not only avoid the mistakes but be stimulated to find the answer to our unsolved

medical problems. Such an organization as ours has proved to be, together with similar societies all over the country, has the future of medicine in its hands.

Such progress made under a free system proves that if we are alert to take the initiative we can direct the changes that are on the way and preserve to our country and its people the best in medical practice.

In conclusion let me enumerate some of the notable direct or indirect contributions that Worcester County has made to medicine.

Here Dorothy Dix of Worcester taught the world compassion for the insane, and here was built the first state-controlled hospital for these unfortunates. From Oxford came Clara Barton of the Red Cross and Dr. Elliott P. Joslin, with his contributions to the treatment of diabetes. It was Charlton that gave Dr. William Morton, discoverer of surgical anesthesia, to the world. In Rutland the first state hospital for tuberculosis was built.

The society has been directly responsible for many activities that have or will spread their influence over the county, state and Nation. It was among the first to raise the standards of medical education. It forced the Massachusetts Medical Society to open its doors to statewide membership.

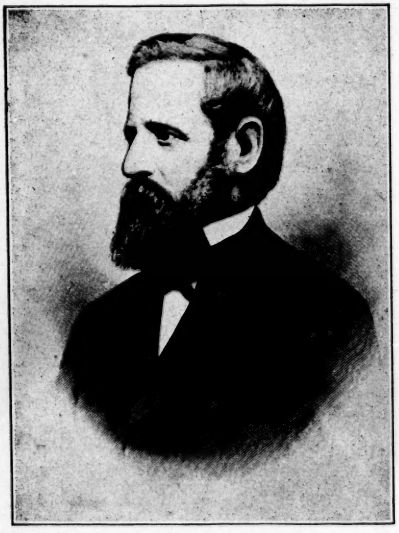

FIGURE 8. *Harrison Bliss.*

Under its leadership, Worcester was one of the first municipalities to establish a laboratory for the diagnosis of diphtheria and tuberculosis. It organized a medical milk commission that pointed the way to combat the terrible infant mortality during the summer months. It has overcome the menace from diphtheria. It publishes a medical

FIGURE 9. *Dr. Charles W. Wilder, of Leominster.*

bulletin, the first of its kind in Massachusetts. Finally it established a blood bank that is supplying both civilian and army needs.

I am indebted to Mr. Matthew Carrigan for the illustrations.

BIBLIOGRAPHY

Burrage, W. L. *A History of Massachusetts Medical Society*, 1781-1922. 505 pp. Boston: privately printed, 1923.

Gage, H. Forty years' progress and problems it has brought to Worcester District Medical Society. The Annual Oration delivered before the Worcester District Medical Society on May 11, 1904.

Getchell, A. C. History of Worcester District Medical Society. A series of articles appearing in *Worcester Medical News* in 1937 and 1938.

Lincoln, W., and Hersey, C. *History of Worcester*. 448 pp. 311 pp. (Part I) and 315-448 (Part II) Worcester, Massachusetts: privately printed, 1862. Pp. 352-359.

Miller, L. C. A survey of hospitals of Worcester District. The Annual Oration delivered before the Worcester District Medical Society on May 8, 1928.

Norwood, W. P. *Medical Education in the United States before the Civil War*. 487 pp. Philadelphia: University of Pennsylvania Press, 1944.

Shattuck, A. M. Fifty years' history of Worcester District Medical Society. The Annual Oration delivered before the Worcester District Medical Society on May 11, 1927.

Ward, R. J. Evolution or revolution. The Annual Oration delivered before the Worcester District Medical Society on May 8, 1935. *New Eng. J. Med.* 213:757-760, 1935.

Idem. Control and hospitalization of contagious diseases. A paper presented at the September, 1940, meeting of the Worcester District Medical Society.

Woodward, L. F. Changes recurring in past twenty-five years having effect on practice of medicine. The Annual Oration delivered before the Worcester District Medical Society on May 9, 1906.

Woodward, S. B., Worcester medical history. In *Hurd's History of Worcester County*. Vol. II. Pp. 885-1762. Philadelphia: J. W. Lewis and Company, 1889. Pp. 1554-1574.

Idem. Secretaries' records of Worcester Medical Society, 1794-1900. The Annual Oration delivered before the Worcester District Medical Society on May 13, 1896.

Idem. Address to staff of Worcester City Hospital. *New Eng. J. Med.* 215:526-529, 1936.

THE DIFFERENTIATION OF BRONCHIOGENIC CARCINOMA AND PULMONARY TUBERCULOSIS

NAHUM R. PILLSBURY, M.D.,* AND JOSEPH D. WASSERSUG, M.D.†

SOUTH BRAINTREE, MASSACHUSETTS

BECAUSE of the many clinical and roentgenologic similarities of bronchiogenic carcinoma and pulmonary tuberculosis, their differentiation may present certain diagnostic difficulties. Among Overholt's[1] cases of primary cancer of the lung, there were 40 patients who were treated for pulmonary tuberculosis because of an originally erroneous diagnosis. Similarly, Moersch and Tinney[2] reported that in their series of 448 patients with proved bronchiogenic carcinoma, 13 spent several months in tuberculosis sanatoriums before the correct diagnosis was established. It was therefore believed that an analysis of cases of bronchiogenic carcinoma admitted to a tuberculosis hospital might shed additional light on this perplexing diagnostic problem.

Twelve such cases were found during the last ten years; they are summarized in Table 1. All were proved either by bronchoscopy or by post-mortem examination. An approximately equal number of cases were seen in the Diagnostic Clinic of the hospital, and the majority were referred for consultation with a thoracic surgeon. Since these patients were never admitted to the sanatorium, they are excluded from this study. Excluded, too, are all metastatic malignant growths and unconfirmed primary tumors. Two patients (Cases 4 and 11) who had both cancer and tuberculosis have been included.

TABLE 1. *Summary of Proved Cases of Bronchiogenic Carcinoma.*

Case No.	Sex	Age	Side Affected	Period in Hospital	No. of Negative Sputums	Symptoms					Signs	
						Cough	Expectoration	Hemorrhage	Pain	Dullness	Rales	Altered Breath Sounds
		yr.		mo.								
1	M	40	L	5	34	+	+	0	0	+	+	+
2	M	55	R	9	29	+	+	0	+	+	0	+
3	M	66	R	7	29	+	+	+	0	+	+	+
4	M	67	R	2	4	+	+	+	0	+	+	+
5	M	51	R	3	30	+	+	+	+	+	+	+
6	M	51	L	2	15	+	+	+	+	+	+	+
7	M	61	L	1	18	+	+	+	+	+	0	+
8	M	47	R	2	15	+	+	0	+	+	0	+
9	M	57	R	1	6	+	+	0	+	+	+	+
10	M	56	R	2	17	+	+	+	0	+	+	+
11	M	63	R	½	3	+	+	+	0	+	+	+
12	M	68	R	½	4	+	+	0	0	+	0	+

Although these cases form too small a group for statistical analysis, they nevertheless bring out certain diagnostic points that are especially deserving of consideration.

Sex

All the patients were men. Although bronchiogenic carcinoma does occur in women, it is preponderantly a male disease. In Overholt's[1] series, the ratio of men to women was 3.5:1.0. At the Mayo

*Superintendent, Norfolk County Hospital.

†Assistant physician, Norfolk County Hospital.

Clinic[2] this disease was found to occur nearly five times as frequently in males as in females. According to King,[3] 80 per cent of the cases occur in males.

Age

The patients were between forty and sixty-eight years old at the time of their admission to the sanatorium. Although the disease may occur at any age, most cases are found between the fourth and sixth decades of life. Eighty per cent of Moersch and Tinney's[2] patients were more than forty years of age, and the highest incidence of the disease was in the sixth decade. The average age of Overholt's patients was fifty-five years.

Side Affected

In 9 of these 12 cases the disease was in the right bronchial tree. According to Betts,[4] 31 of his 46 patients with so-called "central tumors" had right-sided involvement. Moersch and Tinney[2] found the disease twice as often on the right side as on the left.

Symptoms

Bronchiogenic carcinoma presents no characteristic syndrome. This point cannot be overemphasized. Of the complaints most frequently elicited — cough, expectoration, hemorrhage and pain — all or any of these symptoms may occur in almost any combination both in bronchiogenic carcinoma and in chronic infectious diseases of the lungs. Hemoptysis may or may not be present. Pain may be entirely absent, or it may be exceedingly severe if the pleura, nerves or thoracic cage is involved by extension or metastases. All the patients in this series had a productive cough, but neither the character of the cough nor the gross appearance of the sputum was distinguishable from that found in many other pulmonary disorders.

TABLE 1. *Summary of Proved Cases of Bronchiogenic Carcinoma (Continued).*

Case No.	X-Ray Findings			Diagnosis Confirmed		Comment
	Infiltration	Atelectasis	Cavitation	Bronchoscopy	Autopsy	
1	+	0	+	0	+	This case was diagnosed as lung abscess. Thoracotomy and thoracoplasty were performed. The patient left the hospital at his own request, and died 20 days later at another hospital.
2	0	+	0	+	0	Bronchiogenic carcinoma was suspected on admission. The patient was bronchoscoped 29 days later. Metastatic cervical lymph nodes were discovered 12 days after bronchoscopy.
3	+	0	0	0	+	The patient was too ill for bronchoscopy. There was almost constant hemorrhage.
4	+	0	+	0	+	On admission there was a metastatic nodule on the anterior abdominal wall. Two sputum specimens were positive for tuberculosis. Autopsy confirmed both tuberculosis and cancer.
5	+	0	+	0	+	Destruction of ribs was noted by x-ray 1 month after admission. Metastases were found on post-mortem examination.
6	0	+	0	+	+	Malignancy was suspected on admission. Bronchoscopy was performed 31 days later. The patient died while awaiting transfer to a cancer hospital.
7	0	+	0	+	0	A bronchogram was taken 8 days after admission. A diagnosis of carcinoma was made clinically and by x-ray. Bronchoscopy was performed 1 month after admission.
8	0	+	+	0	+	The diagnosis of bronchiogenic carcinoma was made on admission. The patient was very ill: also had bronchiectasis.
9	0	+	0	+	0	Carcinoma of the bronchus was suspected on admission. Bronchoscopy, 21 days later, showed carcinoma in the right main-stem bronchus.
10	0	0	+	+	0	The patient was admitted for observation. Bronchoscopy was performed 1 month later. Infiltration of the trachea was seen, and mediastinal metastases were suspected.
11	+	0	+	0	+	The patient had tuberculosis of the right hand. Both pulmonary tuberculosis and bronchiogenic carcinoma were found at autopsy.
12	0	+	0	+	0	The patient was admitted for observation. Bronchoscopy, 1 day after admission, disclosed bronchiogenic carcinoma, with probable metastases.

The absence of pathognomonic symptoms in carcinoma of the lung has been stressed by Fetter,[5] Overholt[1] and others. Of the group of cases reported by Moersch and Tinney,[2] 5 per cent had, indeed, no symptoms referable to the thorax.

Signs

The physical findings in the thoracic examination depend primarily on the size and situation of the tumor. The signs are therefore exceedingly variable, and this point has also been stressed by other writers. In the present series, dullness of some degree and alterations in breath sounds were noted in every case. Rales, often apical, were detected in 8 cases.

X-Ray Diagnosis

The x-ray diagnosis of bronchiogenic carcinoma has recently been discussed in detail by Holmes[6] and Scatchard.[7] Overholt[1] has also included in his paper excellent reproductions of roentgenograms that illustrate how closely this disease may simulate pulmonary tuberculosis. Any combination of the roentgenologic findings characterized as infiltration, atelectasis or cavitation may be present. Half the cases in the present series had cavitation on their admission x-ray films.

In regard to x-ray diagnosis, Moersch and Tinney[2] wisely point out, "It is also important to remember that a negative roentgenogram does not definitely rule out the presence of carcinoma." If symptoms are suggestive and persistent, a negative roentgenogram should not deter one from further diagnostic studies.

Bronchoscopy

Betts,[4] in a thorough discussion of the subject, has called bronchoscopy "the most important method of diagnosis in primary carcinoma of the lung." To be of value from a therapeutic standpoint, however, bronchoscopy must be performed early in the course of the disease. Usually the progress of bronchiogenic carcinoma is rapid, its duration being measured in months. The delay between the time the disease is first suspected and the time of bronchoscopy — or some other definitive diagnostic study — should be counted in days, not in weeks or months.

In half these cases the diagnosis was made by bronchoscopy, and the interval from admission to bronchoscopy varied from one day to one month. Two patients (Cases 3 and 8) were too ill for bronchoscopic examination; two other (Cases 4 and 5) had evident metastases. In 1 case (Case 1), seen in 1934 and not bronchoscoped, the diagnosis was missed clinically and made only at post-mortem examination.

Discussion

Patients with bronchiogenic carcinoma are occasionally admitted to a sanatorium either for observation for tuberculosis or because a definite diagnosis of tuberculosis has already been made. This is not surprising since, clinically, lung cancer may closely resemble tuberculosis. For this reason reliance must be placed on other diagnostic aids, such as x-ray examination, bronchoscopy and exploratory thoracotomy. Since the x-ray film itself may also be misleading, bronchoscopic examination is of the utmost importance.

Bronchiogenic carcinoma must be *promptly* differentiated from tuberculosis, since time and rest never cure a malignant growth. Waiting six weeks or longer for results of animal inoculation tests or cultures of sputum may rob the patient of his chance of surgical cure.

An early diagnosis of bronchiogenic carcinoma can be made only if the disease is suspected and considered in the differential diagnosis. The possibility of cancer must be given special consideration if the patient is a man between forty and sixty years of age. In all cases in which thoracic symptoms are present, x-ray examination of the chest should be made immediately. If, on the basis of physical and x-ray examination, the disease cannot be differentiated from pulmonary tuberculosis and a few specimens of sputum are negative, bronchoscopy should be performed without further delay. Inspection of the bronchi, if the patient's general condition admits it, yields valuable information that may determine not only the diagnosis but also how the case is to be managed. This is as true of pulmonary tuberculosis as it is of bronchiogenic carcinoma, since the presence or absence of endobronchial tuberculosis may alter plans for collapse therapy. Hence, in either disease much may be gained by prompt bronchoscopic examination.

Summary

Twelve proved cases of patients with bronchiogenic carcinoma who were admitted to a tuberculosis hospital are presented. The clinical and roentgenologic similarities between carcinoma and tuberculosis of the lung are pointed out, and the diagnostic role of bronchoscopy is emphasized.

References

1. Overholt, R. H. Common masquerading lung disease. *Dis. of Chest.* **9**:197-211, 1943.
2. Moersch, H. J., and Tinney, W. S. Carcinoma of lung. *Minnesota Med.* **26**:1046-1051, 1943.
3. King, D. S. Primary cancer of lung. *New Eng. J. Med.* **219**:828-833, 1938.
4. Betts, R. H. Carcinoma of lung: bronchoscopic aspects. *New Eng. J. Med.* **225**:519-525, 1941.
5. Fetter, F. Carcinoma of lung: review of 31 proved cases at Philadelphia Naval Hospital. *Ann. Int. Med.* **18**:978-987, 1943.
6. Holmes, G. W. Carcinoma of bronchus. *New Eng. J. Med.* **227**:503-508, 1942.
7. Scatchard, G. N. X-ray diagnosis of bronchogenic carcinoma. *New York State J. Med.* **44**:617-620, 1944.

CLINICAL NOTE

THERMAL BURNS IN DIABETES MELLITUS*

HOWARD F. ROOT, M.D.†

BOSTON

THE recent report of Taylor, Levenson and Adams[1] emphasizes the marked hyperglycemia found in nondiabetic patients suffering severe thermal burns that involve 2 to 75 per cent of the body surface. Death occurred in 14 of their 35 cases. It is instructive to compare the metabolic changes when serious burns occur in diabetic patients in whom there is a known deficiency in insulin. For this reason, the following cases are reported to illustrate the effects of burns from hot water and from the sun's rays.

CASE 1 (4541). A 66-year-old housewife had diabetes of 7 years' duration. A leg had been amputated for gangrene on February 12, 1925, and the other leg on August 29, 1930. Although insulin had been used for a brief period at the times of operation, the diabetes was of the typically mild degree often associated with gangrene. She had therefore not regularly taken insulin, and the urine was sugar-free with diet alone. The fasting blood-sugar level had varied from 110 mg. to 210 mg. per 100 cc.

On June 11, 1931, while the patient was sitting in a wheel chair washing dishes, boiling water was spilled on her arm and back. Vomiting followed for 3 days. On June 15, she entered the Deaconess Hospital with a second-degree burn on the right arm and a large eschar on the left buttock, the site of the worst burn. She was prostrated, and although not unconscious was in severe acidosis. The blood-sugar level was 480 mg. per 100 cc., and the nonprotein nitrogen 47 mg. The carbon dioxide combining power of the venous blood was 19 vol. per cent, and rose to 27 vol. in 10 hours with 55 units of insulin.

The patient received 195 units of insulin in the first 2 days. On the 10th day, the blood-sugar level was 80 mg., and the nonprotein nitrogen 33 mg., and only 30 units of insulin was required. The urine still showed much albumin. The patient was at times irrational. At first the burns showed no evidence of serious sepsis but this later developed and she died on the 19th day.

CASE 2 (3376). A 35-year-old clerk had diabetes of 15 years' duration when he returned in 1938 for a second period of observation. In 1923 his diabetes was so mild that he required only dietary treatment for the urine to be sugar-free.

In May, 1937, he had a severe sunburn on the shoulders and back; the skin became infected, with the formation of multiple carbuncles. Presumably as a result of bacteremia, he developed phlebitis and osteomyelitis of the right leg, which necessitated a mid-thigh amputation in December, 1937. In this same month, prostatic and paranephric abscesses were found, and the paranephric abscess was drained in January, 1938.

On admission to the New England Deaconess Hospital on March 3, 1938, an inguinal abscess was present, which was drained. The patient still had marked pyuria. The white-cell count was 30,000. The urine contained 1.8 per cent sugar, and the fasting blood sugar was 150 mg. per 100 cc. He was given daily doses of 10 units of crystalline and 40 units of protamine zinc insulin. Recovery was uneventful, and with the exception of a recurring abscess in the inguinal region in September, 1938, from which recovery occurred, he has done reasonably well following a diabetic diet and taking insulin as indicated.

Comment. The instructive feature in his case is the fact that during the period when he suffered severe sunburn and carbuncles developed, his diet was not weighed or measured and the urine was not sugar-free. The failure to control the diabetes may well have been an important factor encouraging the spread of infection, which ultimately led to an amputation of the leg, paranephric abscess and prostatic abscess.

Among the factors contributing to the increased blood sugar in the nondiabetic patients of Taylor, Levenson and Adams, increased glycogenolysis in the liver was mentioned. Another possible source of the extra blood sugar was considered to be glucogenesis from protein, since it has been shown that after thermal burns there is an early increase in protein metabolism. It is possible to add one other factor in discussing the causes of the change in the blood-sugar level, namely, the part played by the skin itself.[2] The skin normally contains much glycogen and some glucose. In diabetic patients with poor control, the normal glycogen stores are greatly reduced but the glucose is increased. This is also true with severe infections involving diabetic patients. When the blood-sugar level is high, it is possible for as much as 20 or 25 gm. of glucose to be present in the skin, and therefore if large areas of the skin are injured, liberation of glucose from the skin may contribute a material increase in blood sugar. In the cases of Taylor, Levenson and Adams, the administration of 25 gm. of glucose intramuscularly was followed by evidence of its utilization within two hours. In nondiabetic patients endogenous insulin is available, but in diabetic patients the lack of normal insulin reserve might result in quite different changes in the blood and tissue chemistry.

81 Bay State Road

*From the New England Deaconess Hospital.

†Associate in medicine, Harvard Medical School; physician-in-chief, New England Deaconess Hospital.

REFERENCES

1. Taylor, F. H. L., Levenson, S. M., and Adams, M. A. Abnormal carbohydrate metabolism in human thermal burns: preliminary observations. *New Eng. J. Med.* 231:437-445, 1944.
2. Joslin, E. P., Root, H. F., White, P., and Marble, A. *The Treatment of Diabetes Mellitus.* Seventh edition. 783 pp. Philadelphia: Lea & Febiger, 1940. Pp. 528 and 529.

MEDICAL PROGRESS

HEMATOLOGY (Concluded)

WILLIAM DAMESHEK, M.D.*

BOSTON

ANEMIA DUE TO BONE-MARROW DISTURBANCES

Anemia due to a disturbance in the bone marrow is usually normochromic (normal color index) and normocytic (normal cell volume and normal cell diameter) because what red cells are produced by the more or less incapacitated marrow are normal from the standpoints of hemoglobin content and cell size. Leukopenia and thrombocytopenia are usually associated phenomena; in other words, there is a *pancytopenia*.

The presence of pancytopenia — anemia, leukopenia, granulocytopenia and thrombocytopenia — should at once lead to the suspicion that a condition involving the bone marrow is present. In general, the diagnostic possibilities are as follows: hypoplasia or aplasia of the marrow, as a rule due to chemicals, at times of idiopathic nature and occasionally associated with myxedema or nephritis; replacement of the marrow by abnormal cells, as in leukemia, lymphosarcoma, reticulosis, Gaucher's disease and fibrosis; so-called "maturation arrest," as seen in liver-extract deficiency; and diminished delivery, usually due to hypersplenism. In the last, although the marrow is normal, in fact hypercellular, the peripheral blood contains fewer red cells, white cells, and platelets than normal. Many of these cases are associated with outspoken splenomegaly. In some, the spleen, although not enlarged, is hyperactive and thus results in an undue inhibitory effect on the bone marrow. This indicates a hormonal relation between the spleen and the bone marrow.

These cases — except those due to pernicious anemia* — are almost always refractory to therapy with liver extract, iron and so forth. Bomford and Rhoads[18] have for this reason grouped them all together in the single designation "refractory anemia," hardly a scientific term for such diverse bone-marrow pictures. My own feeling is that a serious attempt should be made in these cases to establish, so far as possible, an etiologic or at least a pathologic diagnosis. Chronic nephritis and myxedema should be ruled out by appropriate measures. The question of a more or less occult hemolytic process should be gone into by studies of the blood bilirubin, of the output of bile pigments, particularly in the feces, and of the reticulocyte level. But the central point in diagnosis is the sternal-marrow biopsy. A preliminary puncture is performed. If good flecks of marrow are obtained, giving a clear-cut picture in the stained smears, no further testing of the marrow is required. If, however, the material aspirated is minimal in amount and contains few marrow cells, a trephine biopsy should be carried out. It is by no means necessary to remove — as is so often done — a large section of sternum through a 5-cm. or 7-cm. incision. An incision 1 or 2 cm. in length is entirely satisfactory with the use of a trephine with a head 5 to 7 mm. in diameter.

A series of excellent articles on the subject — even though the condition is, unfortunately, referred to as "refractory anemia" — is that by Davidson, Davis and Innes.[19] These studies are characterized by careful marrow examinations and by classification of the various cases as anemias with hypocellular, normoblastic marrows, those with cellular marrows and so forth. In the group characterized by hypocellular, normoblastic sternal marrows, 4 were secondary to chemical exposure but the remaining 12 were idiopathic. Of these 16 cases, 9 were progressive and fatal within the period of a few months. In the cases with a hypercellular megaloblastic marrow, the response to the persistent use of liver extract, although slow, was nevertheless satisfactory, and for this reason, one must seriously consider that these cases were examples of the relatively refractory type of pernicious anemia that Israëls and Wilkinson[6] have called "achrestic anemia." To put these cases under the nondescript term "refractory anemia" makes the whole thing rather confusing and again illustrates the value of classifying a given case of anemia on the basis of cell size, and of probable etiologic mechanisms. In a more recent paper, Davis and Davidson[20] point to the value of the oral administration of proteolyzed liver in a number of cases of rather atypically refractory pernicious anemia in which injections of liver extract had proved ineffective. One wonders in these cases whether the injectable liver extract was really of a high degree of potency.

Of 89 personally studied cases showing pancytopenia,[21] the largest group — 28 cases, or 31.4 per cent — was made up of examples of aleukemic leukemia. In these, the marrow showed an extreme degree of leukocytic hyperplasia, with the presence of many primitive leukocytes, either of the lymphoid, myeloid or monocytic variety. Thirteen cases were in a closely related category, that is, Hodgkin's disease, lymphosarcoma or multiple myeloma (plasmacytoma). Thus in 89 cases with pancytopenia, the fundamental cause of this symptom complex in almost half the cases was a proliferative disease of one of the three white cell-forming

*Professor of clinical medicine, Tufts College Medical School; visiting physician and hematologist, New England Medical Center.

tissues. Pancytopenia is thus an ominous portent of these grave disorders.

Widespread fibrosis of the marrow may occur either secondarily to such conditions as leukemia, lymphosarcoma and metastatic carcinoma or, more frequently, following protracted polycythemia vera. At times it is associated with marble bone or Albers–Schönberg disease and may then be called "osteopetrosis." Rosenthal and Erf[22] describe 1 such case, together with 17 cases of myelofibrosis secondary to various causes. These cases, which have been described under a veritable welter of names, including leukoerythroblastic anemia, osteosclerotic leukemia, nonleukemic myelosis, leukanemia and agnogenic myeloid metaplasia, have as their distinguishing features the following: anemia and well-marked splenomegaly; bone changes consisting of irregular osteoporosis and osteosclerosis, principally in the femurs; anemia, leukocytosis or leukopenia and thrombopenia; and nucleated red cells and myelocytes, which are present in fair to considerable numbers. The presence of these early red and white cells in association with a progressive anemia bespeaks either an unusually vigorous attempt at blood formation or a rather bizarre and uninhibited type of nonproductive hematopoiesis. This is probably associated with the concomitant myeloid metaplasia of the spleen, which occurs secondarily to the initial bone-marrow fibrosis. Blood formation in the spleen is not an unnatural condition, since it probably represents a reversion to embryonic hematopoiesis; nevertheless, it lacks the normal regulatory influence that the spleen itself usually exerts on the bone marrow. This gives rise to an abnormal type of blood picture, characterized by an excess of normoblasts and myelocytes.

These cases are often difficult if not impossible to differentiate from those of chronic myelogenous leukemia with a subleukemic picture, that is, one in which the leukocyte count falls between 8000 and 20,000. In fact, some of the cases that Jackson, Parker and Lemon[23] have called "agnogenic myeloid metaplasia," that is, myeloid metaplasia arising *sui generis*, may in reality be examples of chronic myelogenous leukemia. That fibrosis of marrow may occur in chronic leukemia has been shown in a careful study by Churg and Wachstein,[24] who, in 97 cases of myeloid leukemia, found 6 showing myelofibrosis. Osteosclerosis is only rarely, if at all, associated with true leukemia. I have recently, however, seen a case that fulfilled all the criteria of myeloid metaplasia of the spleen secondary to myelofibrosis, and with the extensive bone changes of osteosclerosis, in which there were a striking regression in the size of the spleen and a striking improvement in the hemoglobin and erythrocyte values following x-radiation over the spleen. X-ray therapy and splenectomy have been said to be contraindicated because the spleen might be the only available source of hematopoiesis. A trial of x-ray therapy in relatively small doses directed over the spleen seems to be indicated in doubtful cases.

In cases showing pancytopenia and a large spleen, and in which the marrow shows erythroblastic hyperplasia without evidence of leukemia, particularly if some evidences of increased hemolysis are present, one should at least consider the possibility of hypersplenism. Splenectomy in some of these cases has been dramatically successful, not only in raising the red-cell count to normal but also in bringing the low leukocyte and platelet counts to normal values. These cases are closely related to the syndromes of "splenic neutropenia,"[25] acquired hemolytic anemia and idiopathic thrombopenic purpura. The incidence of these cases should materially increase as their possibility is more frequently considered.

Anemias Due to Excessive Loss of Blood

Hemorrhagic Anemia

Many cases treated routinely for months or even years with liver extract, iron and vitamin B complex are found — often too late — to be examples of chronic hemorrhagic anemia, usually secondary to bleeding from the gastrointestinal tract. With a little attention to a few morphologic details in the blood and with more frequent examinations of the stools for occult blood, these cases could doubtless be diagnosed more frequently.

Although the anemia in these cases is usually hypochromic, with color indices in the vicinity of 0.5, I have seen occasional cases with normochromic anemia, particularly when the bleeding was brisk. The white-cell count is usually low (4000 to 6000), but the granulocytes are usually slightly elevated. Stippling may be present. The platelets are usually moderately or greatly increased. The hypochromic anemia indicates a hemoglobin deficiency for the normally developing normoblasts; in association with reticulocytosis and increased platelets, indicating a hyperactive bone marrow, there is a definite likelihood of chronic hemorrhage.

Careful search for cause of the anemia should be instituted. Stool examinations for occult blood and exceedingly careful x-ray examination of the gastrointestinal tract are in order. Possibilities are diaphragmatic hernia, bleeding peptic ulcer, carcinoma of the stomach, carcinoma of the cecum or colon, Meckel's diverticulum, terminal ileitis with hemorrhage and even the lowly hemorrhoid. Lesions of the small bowel are often missed in hurried x-ray examinations, and for this reason, careful fluoroscopy with the spot film technic is invaluable.

Hemolytic Syndromes

Mechanisms. Little is known of the mechanisms of normal blood destruction. The mature nonnucleated red cell, after many trips about the

circulation, probably wears out and is then converted into a denatured protein, bilirubin and iron. Is the spleen truly the graveyard of the normal red cell or does it simply cause the red cells to swell as they stagnate there for variable periods? Do agents of various types — the lysolecithin of Bergenhem and Fahreus, immune hemolysins or agglutinins and various metabolic products — bring about gradual hemolysis? There is at present no answer to these questions.

Since 1940, Johnson and Freeman[26] have been concerned with the hemolytic action of chyle and its possible relation to normal blood destruction. After a fat meal, they state that the circulating red cells become exposed to a sufficiently high concentration of hemolytic material to cause an increase in blood destruction. This was demonstrated by exposing normal red cells to normal and lipemic serums and by observing the degree of hemolysis in both. Lipemic serums, which were obtained from persons who had taken a large amount of cream or corn oil, were slightly, although distinctly, hemolytic. Normally, however, the red cell is protected from an undue concentration of lipemic plasma by several mechanisms, including chiefly the high dilution of the hemolytic chyle that occurs with the large volume of blood in the subclavian vein and heart. Although this mechanism, as postulated by Freeman and Johnson, may well be one factor, a likelier one is probably the purely mechanical action involved in the squeezing and buffeting about which the red cell develops within the capillaries. This factor of mechanical fragility, which was investigated by Miller and myself[27] a few years ago, has more recently been studied by Shen, Castle and Fleming.[28] When normal red cells are shaken in a test tube or other container with glass beads for a given length of time, for example, three hours, a small amount of hemolysis takes place, which varies from 1 to 3 per cent. The mechanical fragility is greatly increased in the presence of an agglutinating agent (see below), which presumably still further injures the rather tough red-cell membrane. One must concede that the mechanisms of normal hemolysis are but little known and must await further elucidation.

In the field of abnormal or increased hemolysis, a number of different mechanisms may operate to destroy the red cell. One may list these as follows: bacterial agents, notably the hemolytic streptococcus; parasites, notably that of malaria and the bartonella of Oroya fever; chemicals, including the sulfonamide drugs and phenylhydrazine; immune hemolysins; agglutinins, cold and warm, usually of the immune-body type; certain physical factors, such as extreme heat and cold; unknown factors; and hypersplenism.

Bacterial agents, parasites and chemicals appear to attack the red cell directly. Hemolysins, as Dameshek and Miller[27] have shown, may be simple or complex. The simple ones hemolyze the red cell directly, whereas those which are complex require the mediation of complement. Thus, with the immune hemolysin that occurs in certain cases of acute hemolytic anemia, the amboceptor has a sensitizing or agglutinating or membrane-injuring role, whereas actual hemolysis is brought about by complement. In other types of hemolytic anemia, the presence of a hemolysin may be noticeable only by the behavior of the red cell. Thus, the small, thick red cell, the spherocyte, which is fragile in hypotonic solutions of sodium chlorides, has probably been already injured by a hemolysin that cannot be detected by any means at present at one's command. The red cell of chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria, which is abnormally fragile to dilute acid and also to heat, is probably abnormal because it has been acted on by a hemolysin, which itself cannot be detected. In paroxysmal cold hemoglobinuria, a well-defined hemolysin can be demonstrated, as first described many years ago by Donath and Landsteiner. This hemolysin requires so-called "sensitization" with cold, then warmth and finally the presence of complement. The chemical nature of hemolysins is almost a completely untouched field.

Agglutinins, by causing red cells to mass together, probably injure the red-cell membrane, as can be readily shown by exposing a red-cell suspension to varying concentrations of agglutinin and then shaking them in a mechanical shaker. The effect of shaking on agglutinated red cells is probably similar to the buffeting that these cells receive in a highly active circulation. In any event, the mechanical fragility of agglutinated red cells is greatly increased over normal (up to 80 per cent in a three-hour period). This is evident in transfusion reactions associated with incompatible blood. The extreme hemolysis, with hemoglobinuria and acute hemolytic anemia, that ensues is due to agglutination, with its injurious effect on the red-cell membranes, and the mechanical activity of an actively moving circulation. This type of agglutinative-hemolytic reaction is also seen in acute hemolytic anemia of the newborn (erythroblastosis fetalis) and in certain cases associated with the presence in the blood of an unusually high concentration of cold hemagglutinins.

The red cell may also be injured by a variety of physical agents, including heat, cold and various light rays. Undue heat, as in a thermal burn, by directly injuring the red cells in superficial capillaries may bring about their quick rupture and thus cause hemoglobinuria or their slower degradation by way of the spherocyte. This is another link in the concept that the spherocyte is a red cell that has been injured by some type of hemolytic agent and has therefore assumed an abnormal, unusually spherical form. This renders the cell unusually vulnerable to hemolysis by either splenic or other mechanisms.

Hypersplenism, in which an undue or abnormal activity of the spleen is postulated, is becoming increasingly evident as a cause of hemolytic anemia. The enlarged spleen of many conditions — portal hypertension, splenic-vein thrombosis, Hodgkin's disease and certain other conditions — may somehow develop an unusual degree of hemolytic activity. These cases are usually accompanied by leukopenia and thrombopenia, both of which are probably due to hypersplenic inhibition, rather than to unusual phagocytosis by splenic cells.

There are probably many other factors that injure the red cells and result in various degrees and types of hemolytic anemia. Hereditary factors involving hemoglobin metabolism and the structure of the red cell, as in Mediterranean target-oval-cell syndromes and in sickle-cell disease, and obscure factors, such as the hemolytic anemia symptomatic of Hodgkin's disease, Boeck's sarcoid and dermoid cyst, are among these totally unknown causes of increased blood destruction. A consideration of the etiologic factors may be distinctly worth while in working out the possible mechanism in a given case of hemolytic anemia and in making the ultimate decision regarding the value of splenectomy as a therapeutic procedure.

Differential red-cell fragility. Red-cell fragility has for many years been associated with the reaction of red cells to hypotonic salt solutions. This test serves only to discriminate between cells showing varying degrees of thickness, the range of hemolysis in a given case indicating the limits of the "thickness population" of the red cells. Normally, some begin to hemolyze in a 0.45 per cent solution of sodium chloride but all become hemolyzed at a 0.25 per cent concentration. Thick red cells — spherocytes — begin to hemolyze at concentrations close to that of normal saline solution, and thin red cells — leptocytes or target cells — are at times incompletely hemolyzed even in solutions containing as little as 0.04 per cent of sodium chloride. An amusing, although sound, article from Honolulu on erythrocyte fragility is that by Fennel,[29] who recommends a simple one-tube "screen test" for determining whether or not abnormal hypotonic fragility is present. A 0.38 per cent solution of sodium chloride is employed, and the degree of hemolysis is measured with the photoelectric colorimeter. If any increase in the normal degree of hemolysis is present, a second or serial dilution test is carried out. The author concludes, "At least, try the one tube of 0.38 per cent saline in conjunction with your routine hematology, and see if you don't get interested."

One should always realize that whatever a red cell shows in its reaction to hypotonicity does not necessarily indicate its reaction within the circulation, where everything is always isotonic. There may, then, be other ways of measuring red-cell vulnerability or fragility.

The question of acid hemolysis or fragility has already been mentioned. In one disease, and apparently in only one, as Ham[30] and others have pointed out, the red cell is unusually vulnerable to dilute acids. A presumptive test may be made with carbon dioxide gas, and the complete test with various types of dilute acids, with and without complement.

The matter of mechanical fragility has also been alluded to. It may be worth while to introduce this method as a more or less routine measure in the study of hemolytic anemias. Mechanical fragility is increased in the presence of warm and cold hemagglutinins (when testing for the latter, the serum must be kept cold) and to some extent in such conditions as sickle-cell and other hemolytic anemias.

Heat fragility has recently been introduced by Hegglin and Maier.[31] This is a simple test in which a tube of clotted blood is placed in an incubator at 37°C. for three to twenty-four hours. Apparently in only one disease, again paroxysmal nocturnal hemoglobinuria, are sufficient red cells hemolyzed with simple incubation to result in hemolysis readily visible to the naked eye. The precaution must be used of taking the blood with a dry syringe and under as little stasis as possible.

One may thus study the resistance of the red cells in a given case of hemolytic disease by at least these four methods and arrive at a more or less etiologic diagnosis. Doubtless, other methods may be used, as Dameshek and Singer[32] suggested some years ago, including resistance to saponin, lecithin, lysolecithin and so forth. The concept of differential fragility serves to indicate that when the red cell is injured by different substances it reacts differently.

Clinical features. As pointed out in previous reviews, three types of *hereditary hemolytic syndromes* may be discriminated: familial spherocytosis (congenital or familial hemolytic anemia or jaundice); Mediterranean target-oval-cell disease (Cooley's anemia, thalassemia, Mediterranean anemia or familial leptocytosis); and sickle-cell anemia. Of these, familial spherocytosis is by far the best known. Mediterranean target-oval-cell disease has been known for some years as a severe, fatal condition. The milder types have only recently been studied (Wintrobe et al.,[33] Dameshek[34] and Smith[35]). These observers have all pointed out the numerous gradations in the types of cases — from the most fatal form, Cooley's anemia, down to the extremely mild cases, in which abnormalities can be demonstrated only by careful hematologic studies. The severest cases show marked anemia, increased hemolysis, splenomegaly, significant bone changes and the presence of numerous nucleated red cells in the circulating blood. Moderately severe cases present moderate anemia, splenomegaly, slight icterus and minimal bone changes. Mild cases show absolutely nothing on physical examination and only slight

hypochromic anemia or erythrocytosis in the blood counts. All types, severe, moderate and mild, show target and oval red cells in varying concentrations and increased resistance of the red cells to hypotonic salt solutions. The red cells are unusually thin, apparently because of a disturbance in hemoglobin synthesis, with the formation of normal-sized cells lacking sufficient hemoglobin for the amount of cytoplasm that is present. Iron therapy is totally ineffective, and hemoglobin values remain surprisingly constant.

These cases are apparently transmitted by a Mendelian dominant mechanism. A careful study of them from the standpoint of the morphology of the blood was made by Valentine and Neel.[36] The mild cases are apparently transmitted by a heterozygous gene, but the severe cases are transmitted through two parents, both bearing this gene. This confirms my own studies,[34] which showed that both parents of patients with severe cases (Cooley's anemia) showed mild target-oval-cell abnormalities. Valentine and Neel point out that this is one of the few diseases in which carriers can be discriminated by careful laboratory studies. These syndromes deserve increasing attention, since they are undoubtedly frequent among Italians and not infrequent among Greeks, Syrians and Portuguese. Anemia, jaundice, splenomegaly, peculiar bone changes and stippling of the red cells occurring in one of these racial groups should always make one consider the possibility of a target-oval-cell syndrome.

More attention is also being paid to sickle-cell disease, which in many respects resembles target-oval-cell disease rather strikingly, and may in fact be related to it. In sickle-cell disease, as in the Mediterranean syndromes, a central feature is the presence of thin, hypotonically resistant, target cells. Hemolysis and splenomegaly are features of the severe cases, and there is no response to the administration of iron, despite the hypochromic character of the anemia. The carriers of the disease may well be those with the sickling trait, who number about 7 per cent of the Negroes in this country. Sickle-cell disease, although almost exclusively limited to those of African origin (colored), also occurs to some extent in Italians and occasionally in Portuguese — apparently without any colored admixture. The highly abnormal sickled cell may be related to the elongated, elliptical cell of the Mediterranean disease.

An interesting study of the occurrence of sicklemia in the black Carib Indian had been made by McGavack and German.[37] The black Caribs are not truly Indians but natives of Honduras who have preserved for centuries the purity of their original racial African stock. Twenty-four (8 per cent) of the 300 persons studied showed the sickling phenomenon. None had apparently had sickle-cell disease, and sickle-cell anemia as such had never been recorded in the local hospital.

Murphy and Shapiro[38] describe a new technic for demonstrating the sickling trait. By this method the process of sickling can be readily studied from the stage of the normal flexible red cell to the stage of sickling when flexibility is lost and the cell appears "as fixed and rigid as a crystal of ice as it moves about and abuts against cells and fixed objects." These and other observations led Murphy and Shapiro to conclude that the dissociation of combined hemoglobin bears a causal relation to the phenomenon of sickling. Because of its rigidity within the circulation, the sickled cell may be unusually vulnerable to mechanical trauma (mechanical fragility).

Winsor and Burch[39] showed that the sedimentation rate in sickle-cell anemia may be used as a diagnostic measure. By oxygenating sickle-cell blood the sedimentation rate increases, and by adding carbon dioxide to the blood the rate decreases. Instead of adding carbon dioxide to the blood, one may study the sedimentation rate of blood taken with and without stasis by means of a tourniquet applied for six minutes. The lability of the sedimentation rate with respect to oxygen and carbon dioxide and the relation of the different rates to each other are said by the authors to comprise a "diagnostic parameter." If the difference between the two sedimentation rates is greater than 20 mm. per hour, the patient has sickle-cell anemia.

Bauer and Fisher[40] describe a nonanemic variety of sickle-cell disease. All Negro patients should be routinely tested for sicklemia to avoid such erroneous diagnoses as rheumatic fever, rheumatic heart disease, polyarthritis and cerebral disease. The authors report 6 cases in which the pathologist diagnosed the condition post mortem; in 5 of these the clinician had not even suspected the condition. Brugsch and Gill[41] report 4 cases of sickle-cell anemia in which the diagnosis was obscured by the presence of polyarthritis and heart murmurs simulating rheumatic fever. Italians, too, may have symptoms simulating various conditions but which in reality are due to sickle-cell disease. Thus Canby, Carpenter and Ellmore[42] report a case in which an apparently acute surgical condition of the abdomen in a youth of pure Sicilian stock was due to multiple infarctions of the spleen. Splenectomy was performed, and later sickle-cell anemia was discovered. Reinhard, Moore, Dubach and Wade[43] describe the results of a careful study of the effects of high concentrations of inspired oxygen in patients with sickle-cell anemia. Although a decrease in the degree of intravascular sickling of the red cells occurred, there was no consistent detectable change in the rate of hemolysis. In fact, erythrocytogenesis was depressed by the oxygen therapy, both the reticulocytes and the red cells being decreased; when

oxygen was discontinued, a striking increase in reticulocytes occurred.

A good review article on the *acquired hemolytic syndromes* is that by Davis.[44] Acute hemolytic anemia following the administration of sulfadiazine is often accompanied by the presence in the blood serum of a cold hemagglutinin. This has been commented on, among others, by Layne and Schem[45] and by myself.[46] The exact relation of the cold hemagglutinin to the drug and to the hemolytic anemia is obscure. Its presence in high titer may lead to a false interpretation of "incompatibility" in testing the patient's serum with prospective donor's red cells prior to transfusion. This may readily be obviated by performing the cross-match according to Landsteiner's test-tube method at incubator temperature. The blood should be warm when administered; if bank blood is used, it should be allowed to warm at room temperature for two or three hours. Stats[47] studied 2 cases in which extremely high titers of cold hemagglutinin were present, demonstrating the importance of mechanical trauma as a cause of hemolysis in agglutinated red cells. This is in line with the previous work of Dameshek and Miller[27] showing the injurious effect of agglutinin on the red-cell membrane and the importance of mechanical trauma as a cause of hemolysis whenever a hemagglutinin in sufficiently high titer is present. This is presumably true not only in patients with a cold hemagglutinin but also in transfusion accidents due to incorrect cross-matching and to the presence of an anti-Rh agglutinin (Rh-factor reaction). The red cells are injured when they become agglutinated, and being present in agglutinated masses, they are vulnerable to the constant buffeting about in an active circulation. Intravascular hemolysis then takes place, with resultant hemoglobinemia and hemoglobinuria. Masses of acid hematin are usually precipitated in the renal tubules, and nephropathy follows. A case of chronic hemolytic anemia with autoagglutination and hyperglobulinemia is reported by Kracke and Hoffman.[48] A similar case was recently studied by Katz and myself.[49] Hyperglobulinemia was also present and was presumably due to the exceedingly high titer of cold hemagglutinin, which was 1:500,000. Intravascular agglutination could be readily demonstrated by microscopic examination of the capillaries at the nail bed and in the cornea. Hemoglobinemia occurred when a whole arm was immersed in iced water.

Acute hemolytic anemia of the newborn (erythroblastosis fetalis) has now been firmly established as due to a reaction between the Rh antibody (anti-Rh agglutinin) and the Rh factor or agglutinogen. Levine,[50] whose pioneer work in this field is outstanding, presents a review of the pathogenesis of the disease. In this paper, the technics of agglutination tests and their interpretation, the varieties of human anti-Rh serum, the matter of the so-called "Hr factor" as it occurs in mothers who are Rh+, familial and racial factors and the treatment with transfusions of Rh− blood are discussed. This article will repay careful reading. Another excellent and comprehensive review is that by Potter.[51] Comments concerning the laboratory problems involved in Rh-factor testing are presented by Kracke and Platt.[52] These are often difficult. The clinician reading a report of "Rh−" or "Rh+" rarely knows the difficulties that are often encountered in the laboratory in making the decision. Too many weak serums are on the market that give false negative reactions. Until a good animal or other method is developed for preparing anti-Rh serum, these difficulties will doubtless continue. The other big problem is the possibility of developing some method for neutralizing the mother's anti-Rh agglutinin so that it cannot agglutinate the fetus's Rh+ red cells. Until this comes about, the erythroblastotic-producing mother is faced with the constant and recurring threat, with each new pregnancy, of the development in the fetus of hydramnios, acute hemolytic anemia, severe jaundice and so forth.

The *idiopathic hemolytic anemias*, unassociated with agglutinins or reactions to drugs, are of great interest. I have recently seen an increasing number in which the spleen seemed to be the central feature of the disease and the resulting hypersplenism the cause of the hemolytic anemia, the leukopenia and the thrombopenia. The mechanisms by which the spleen in these cases gives rise to increased hemolysis are quite obscure. The leukopenia and thrombopenia may be explainable by an unusual degree of inhibition of the bone marrow by an overactive spleen. Splenectomy is usually — not always — followed by a dramatic rise in the red-cell count to a normal or increased value. I[53] have discussed the physiologic pathology and the therapy of these cases in a recent article.

113 Bay State Road

References

18. Bomford, R. R., and Rhoads, C. P. Refractory anaemia: clinical and pathological aspects. *Quart J. Med.* **10**:175-234, 1941.
19. Davidson, L. S. P., Davis, L. J., and Innes, J. Studies in refractory anaemia. *Edinburgh M. J.* **50**:226-236, 355-377 and 431-443, 1943.
20. Davis, L. J., and Davidson, L. S. P. Proteolysed liver in treatment of refractory anaemias. *Quart J. Med.* **13**:53-73, 1944.
21. Dameshek, W., and Katz, H. Unpublished data.
22. Rosenthal, N., and Erf, L. A. Clinical observations on osteopetrosis and myelofibrosis. *Arch. Int. Med.* **71**:793-813, 1943.
23. Jackson, H. Jr., Parker, F. Jr., and Lemon, H. M. Agnogenic myeloid metaplasia of spleen: syndrome simulating other more definite hematologic disorders. *New Eng. J. Med.* **222**:985-994, 1940.
24. Churg, J., and Wachstein, M. Osteosclerosis, myelofibrosis and leukemia. *Am. J. M. Sc.* **207**:141-152, 1944.
25. Wiseman, B. K., and Doan, C. A. Primary splenic neutropenia: newly recognized syndrome, closely related to congenital hemolytic icterus and essential thrombocytopenic purpura. *Ann. Int. Med.* **16**:1097-1117, 1942.
26. Johnson, V., and Freeman, L. W. Hemolytic action of chyle. *Am. J. Physiol.* **130**:723-728, 1940.
27. Dameshek, W., and Miller, E. B. Pathogenetic mechanisms in hemolytic anemias. *Arch. Int. Med.* **72**:1-17, 1943.
28. Shen, S. C., Castle, W. B., and Fleming, E. M. Experimental and clinical observations on increased mechanical fragility of erythrocytes. *Science* **100**:387-389, 1944.
29. Fennel, E. A. Erythrocyte fragility. *Am. J. Clin. Path.* (Tech. Sect.) **8**:21-26, 1944.
30. Ham, T. H. Studies on destruction of red blood cells: chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria: investigation of mechanism of hemolysis, with observations on 5 cases. *Arch. Int. Med.* **64**:1271-1305, 1939.
31. Hegglin, R., and Maier, C. "Heat resistance," of erythrocytes: specific test for recognition of Marchiafava's anemia. *Am. J. M. Sc.* **207**:624-626, 1944.

32. Dameshek, W., Schwartz, S. O., and Singer, K. Sphero cytosis (and increased erythrocyte fragility) as indicators of hemolytic activity, with consideration of "differential" fragility. *J. Clin. Investigation* **18**:479, 1939.
33. Wintrobe, M. M., Matthews, E., Pollack, R., and Dobyns, B. M. Familial hemopoietic disorder in Italian adolescents and adults resembling Mediterranean disease (thalassemia). *J. A. M. A.* **114**: 1530-1538, 1940.
34. Dameshek, W. "Target cell" anemia. Anerythroblastic type of Cooley's erythroblastic anemia. *Am. J. M. Sc.* **200**:445-454, 1940. Familial Mediterranean target-oval cell syndromes. *Ibid.* **205**: 643-660, 1943.
35. Smith, C. H. Familial blood studies in cases of Mediterranean (Cooley's) anemia: diagnosis of trait, or mild form of disease. *Am. J. Dis. Child.* **65**:681-701, 1943.
36. Valentine, W. N., and Neel, J. V. Hematologic and genetic study of transmission of thalassemia. *Arch. Int. Med.* **74**:185-196, 1944.
37. McGavack, T. H., and German, W. M. Sicklemia in black Carib Indian. *Am. J. M. Sc.* **208**:350-355, 1944.
38. Murphy, R. C., Jr., and Shapiro, S. Sickle cell disease. 1. Observation on behavior of erythrocytes in sickle cell disease. *Arch. Int. Med.* **74**:28-35, 1944.
39. Winsor, T., and Burch, G. E. Diagnostic physicochemical blood tests in sickle cell anemia. *Am. J. M. Sc.* **207**:152-160, 1944.
40. Bauer, J., and Fisher, L. J. Sickle cell disease with special regard to its nonanemic variety. *Arch. Surg.* **47**:553-563, 1943.
41. Brugsch, H. G., and Gill, D. Polyarthritis in sickle-cell anemia. *New Eng. J. Med.* **231**:291, 1944.
42. Canby, C. E., Carpenter, G., and Ellmore, L. F. Drepanocytosis (sicklemia) and apparently acute surgical condition of abdomen: report of their occurrence in white youth, with laparotomy. *Arch. Surg.* **48**:123-125, 1944.
43. Reinhard, E. H., Moore, C. V., Dubach, R., and Wade, L. J. Depressant effects of high concentrations of inspired oxygen on erythrocytogenesis: observations on patients with sickle cell anemia with description of observed toxic manifestations. *J. Clin. Investigation* **23**:682-698, 1944.
44. Davis, L. J. Haemolytic anaemias (Honyman Gillespie lecture). *Edinburgh M. J.* **50**:589-616, 1943.
45. Layne, J. A., and Schemm, F. R. Acute macrocytic hemolytic anemia occurring following administration of sulfadiazine. *J. Lab. & Clin. Med.* **29**:347-351, 1944.
46. Dameshek, W. Cold hemagglutinins in acute hemolytic reactions in association with sulfonamide medication and infection. *J. A. M. A.* **123**:77-80, 1943.
47. Stats, D. Cold agglutinated erythrocytes: hemolytic effect of shaking. *Proc. Soc. Exper. Biol. & Med.* **54**:305, 1943.
48. Kracke, R. R., and Hoffman, B. J. Chronic hemolytic anemia with autoagglutination and hyperglobulinemia: report of fatal case. *Ann. Int. Med.* **19**:673-684, 1943.
49. Katz, H., and Dameshek, W. Unpublished data.
50. Levine, P. Pathogenesis of erythroblastosis fetalis: review. *J. Pediat.* **23**:656-675, 1943.
51. Potter, E. L. Present status of Rh factor. *Am. J. Dis. Child.* **68**:32-58, 1944.
52. Kracke, R. R., and Platt, W. R. Clinical significance of Rh factor with comments concerning laboratory problems. *Ann. Int. Med.* **20**:559-569, 1944.
53. Dameshek, W. Management of acute hemolytic anemia and hemolytic crisis. *Clinics* **2**:118-165, 1943.

Correction. In the review of medical progress "Parenteral-Fluid Therapy. I. Estimation and provision of daily maintenance requirements," by Drs. Allan M. Butler and Nathan B. Talbot, which appeared in the October 26, 1944, issue of the *Journal*, the figure "10" in Column A of Figure 3, which specifies the volume of 5 per cent amino acids, should be changed to "110."

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31101

PRESENTATION OF CASE

First admission. A fifty-four-year-old practical nurse was admitted to the hospital because of progressive muscular weakness and a skin eruption.

Five months prior to admission the patient began to feel weak, fatigued easily and perspired excessively. Her symptoms progressively increased. About two months before entry, she developed an erythematous rash on the back of the neck and around the fingernails. This gradually involved the forehead, the perinasal regions, the ears and chin, the arms and the dorsal aspects of both hands. It was associated with slight itching, and there was deep tenderness on pressure over these areas. There was no history of exposure to drugs or chemicals, nor had there been any recent exposure to sunlight. About five weeks before entry she developed gradually increasing edema of both eyelids and exhaustion became so marked that she was forced to stop working. In the month before admission muscular weakness increased to the point where the act of combing the hair on dressing herself required considerable effort. Pain and stiffness at the base of the neck prevented her from holding the head erect. A sensation of a lump in the throat made swallowing difficult. Her weight fell from about 200 to 180 pounds.

The patient gave a history of intolerance for highly spiced and fried foods for many years. About ten to twelve years previously she had had severe attacks of indigestion and excruciating pain in the right upper quadrant radiating through to the back. These attacks lasted several hours and were associated with vomiting of bitter material. There was no history of jaundice or of clay-colored stools. Two months before admission she was found to have a repeatedly positive Wassermann reaction, for which she had received two injections of Mapharsen.

The patient's mother and two half uncles died of tuberculosis. One of her daughters also had tuberculosis. Her husband had a positive Wassermann reaction.

Physical examination revealed a well-developed and well-nourished woman who appeared acutely ill. There was marked periorbital edema, and some

*On leave of absence.

puffiness over the hands and forearms. An irregular, symmetrical, bright erythematous eruption, sharply demarcated from the surrounding skin, was present over the forehead, perinasal area, cheeks and chin. A more diffuse, pigmented eruption was present over the neck posteriorly and on the abdomen. The hands, forearms and shoulders revealed a raised, red, papular eruption, both discrete and confluent, which was most pronounced on the extensor surfaces and around the nails. The lungs were clear, and the heart, except for a soft blowing systolic murmur over the entire precordium, was normal. Neurologic examination revealed some muscular weakness of the back, the arms and, to a lesser degree, the legs. There was no evidence of atrophy, ataxia or tremor. The gag reflex was absent on the right and practically absent on the left. All the deep tendon reflexes were present and equal. Sensory tests were normal.

The temperature was 98.8°F., the pulse 90, and the respirations 20. The blood pressure was 145 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 4,400,000, with 14.7 gm. of hemoglobin. The white-cell count ranged from 4300 to 8900, with 64 to 74 per cent neutrophils, 18 to 29 per cent lymphocytes, about 6 per cent monocytes and 1 per cent eosinophils. Examination of the urine revealed only a few white cells in the sediment. The serum nonprotein nitrogen level was normal, and the protein 6 gm. per 100 cc. The van den Bergh and cephalin flocculation tests were negative. A bromsulfalein test showed 15 per cent dye retention. The Hinton and Wassermann tests were repeatedly positive. A lumbar puncture revealed clear fluid under an initial pressure equivalent to 165 mm. of water. The Wassermann test was positive, and the gold-sol curve was 0011100000. A heterophil agglutination test, skin tests with trichinella antigen and blood cultures were negative.

A roentgenogram of the chest was normal. A Graham test revealed no filling of the gall bladder with dye, and there was a 4-cm. laminated stone in the area.

Over a period of several months, the patient continued to complain of extreme muscle weakness and ran a low-grade fever, usually below 100°F. A therapeutic test with 0.5 mg. of Prostigmine produced no change in symptoms. The eruption, especially that on the face, shoulder and back, became more pronounced and dusky in color and was associated with some edema about the eyes. Numerous transfusions were given. Several infected decubitus ulcers developed on the buttocks and over the right elbow. These were treated with sulfadiazine and azochloramid packs. About five months after admission the patient began to complain of distressing gas pains and diarrhea, with four to five rather loose stools daily, on which guaiac tests were negative. At that time, examination revealed a firm, slightly movable mass in the right upper quadrant, descending with respiration. A rectal examination revealed a small ulcer on the anterolateral wall, which was confirmed by proctoscopy. The edges were thickened and irregular, and the ulcerated area bled on slight trauma. The mucosa of the remainder of the rectum was finely granular and indurated, but no other ulcers were seen. A biopsy of the ulcerated area revealed acute inflammation.

Following this episode the patient began to improve in appearance and spirits. She received 25 mg. of testosterone propionate intramuscularly every two days, but it was noted that the tendency to the improvement antedated this treatment. A gastrointestinal series was made at the beginning of the eighth hospital month. The patient swallowed the barium mixture without difficulty. The esophagus, stomach and small intestine failed to reveal any definite variation from the normal. The gallstone previously described was still present. A barium enema revealed an area of narrowing at the rectosigmoid junction, extending for a distance of 1 cm. This was never seen to dilate more than 1.5 cm.; it did not change in appearance and revealed no areas of ulceration. No other abnormality was seen.

Following the patient's striking improvement, associated with increase in weight, well-being and ability to get about by herself, she was discharged to a nursing home at the end of the ninth month.

Second admission (five weeks later). A few days after her arrival at the nursing home the patient developed spells of vomiting once or twice daily, usually after meals. These were rapidly followed by loss of strength, and she lost 10 pounds in the interval. The vomitus was never black or bloody, nor was there any jaundice or fever. There was mild constipation. Four days prior to admission she developed severe, diffuse, lower abdominal pain and cramps, relieved by the passage of gas. On several occasions she passed a loose stool, together with considerable gas but no blood. The vomiting continued. On the day prior to entry she developed a fever (about 102°F.) for the first time since her discharge.

Physical examination revealed an emaciated woman in moderate distress. The skin showed dry areas of whitening and brownish pigmentation over the face, chest, back and hands. The musculature was atrophic. The lungs were clear. The abdomen was moderately protuberant and exquisitely tender, especially in the lower quadrants. Rebound tenderness was present, but there was no spasm, nor were any masses palpable. Peristalsis was greatly diminished. There was tenderness over both costovertebral angles. A pelvic examination revealed marked tenderness on manipulation of the cervix. Rectal examination showed a questionable ulceration just inside the sphincter on the anterior wall.

The temperature was 101.6°F., the pulse 100, and the respirations 20. The blood pressure was 110 systolic, 60 diastolic.

Examination of the blood revealed a red-cell count of 5,500,000, with 100 per cent hemoglobin, and a white-cell count of 11,900, with 85 per cent neutrophils, most of which were band forms. The urine was normal. The serum nonprotein nitrogen level was normal, and the protein was 6.6 gm. per 100 cc.

A roentgenogram of the abdomen revealed numerous dilated loops of small bowel, and gas was present in the stomach. X-ray examination of the chest revealed little change in the lung fields, but the heart appeared to have increased in size.

A Miller–Abbott tube was passed into the jejunum, and dextrose in water and normal saline solution were administered intravenously. Sulfadiazine was also administered, together with several transfusions. By the eighth hospital day the temperature was normal, and examination of the abdomen revealed normal peristalsis. Tenderness in the lower quadrants was reduced and she had several normal bowel movements. Hourly films of the small bowel showed slight delay in transit, seven hours being required for the barium to reach the colon. There was no definitely abnormal dilatation of the small bowel when barium was present in the loop, but on some of the films there appeared to be dilatation, mucosal irregularities and loss of pattern before the barium entered the loop.

Two days later the temperature rose to 103.2°F. She passed a stool consisting of mahogany-colored fluid with a ++ guaiac reaction, followed on the next day by a semisolid, brown, guaiac-negative stool. The abdomen was generally tender, with rebound tenderness and mild spasm. Rectal examination revealed several extremely tender shallow ulcerations just inside the anus anteriorly; they had the appearance of fistulas. A Levine tube was passed, and 400 cc. of black watery fluid, becoming thick and tarry, was aspirated. The guaiac reaction on this material was ++++. Many rales were audible over both lung bases, and the pulse was rapid. An x-ray film of the chest, taken with the portable machine, revealed linear areas of increased density in the right upper and left midlung fields. An electrocardiogram revealed low voltage in the standard leads, with flat T_1, low to diphasic T_2, slightly inverted T_3 and inverted T_4; R_1, R_2 and R_3 measured 3, 2 and 2 mm. respectively, and S waves were absent.

The patient rapidly became comatose and died on the fourteenth hospital day.

Differential Diagnosis

Dr. Chester M. Jones: My first reaction to this interesting story was that the total picture might have been due to tuberculosis. We know that the patient had gallstones, on the basis of a history of biliary colic and x-ray evidence of stone. We also know that the patient had syphilis, on the basis of numerous positive serologic tests. Arsenical treatment for syphilis was initiated just about the time that the first skin lesions appeared, and it may be of some interest to speculate on the possible role of arsenic in causing the skin lesions. The exposure to tuberculosis in various members of the family is also of interest. Careful evaluation of the progress of symptoms, which started some months prior to the skin eruption, leads me to believe that the gallstones and the syphilis had nothing to do with the fundamental picture as it unfolded. The possible role of tuberculosis remains to be considered. The patient had a story of almost a year's duration, with marked skin changes, intermittent fever and a final elevation of temperature. Furthermore, there was a definite story of rectal ulceration, and a terminal story of that as well as the picture of peritonitis, which makes me think that she had perforated one of the rectal ulcers or one higher up in the colon. She had a rectal stricture and, in addition, a story from the very beginning of progressive muscular weakness and atrophy. The cause of the terminal hematemesis is obscure.

Is there any single diagnosis, aside from gallstones and syphilis, that covers all the facts? If we tie them all together one has to think in terms of tuberculosis, with skin lesions, with gastrointestinal lesions and possibly, because of the rales in the chest, a hematogenous spread at the last moment and a resultant miliary tuberculosis. I am not entirely happy with such an explanation. Syphilis, it seems to me, could explain this picture by stretching one's imagination to the limit. She could have had a rectal stricture due to syphilis. She had a positive spinal-fluid Wassermann reaction, but there were no signs or symptoms of syphilis of the central nervous system. She had a negative gold-sol curve, and there was no increase in the spinal-fluid cell count or protein. It is hard for me to believe that she had central-nervous-system syphilis. There is no evidence that points strongly to cardiovascular syphilis, and syphilis that would produce rectal stricture, ulcers, bleeding and peritonitis is something that I have not seen. I suppose it can occur, because anything can happen with syphilis; but it is not a logical diagnosis. What other things can cause stricture besides syphilis? We may think of it in terms of lymphogranuloma inguinale, but the remaining symptoms are not those of this disease.

If we start with the skin lesions, which I am not qualified to discuss, I should merely say that the erythematous lesions appeared rather suddenly, with muscular weakness, periorbital edema, loss of weight and gastrointestinal symptoms that for the moment we shall leave out. One has to think of lupus erythematosus disseminatus, scleroderma and dermatomyositis. These three diseases ought to be considered in view of the peripheral mani-

festations. I think possibly that each of these conditions could cause that part of the picture. No skin biopsy was taken, although she was in the hospital for nine months; at least there is no record. If it was diagnostic, it may have been omitted purposely. Skin and muscle biopsies of dermatomyositis at the proper stage of the disease, which, as I understand it, is late in the course of the disease, are distinctive and show a degenerative process. There is edema around the muscles, and subcutaneous edema, which can be demonstrated histologically as well as clinically. In scleroderma one observes edema under the skin and thickening, but not the histologic picture of muscular degeneration that is seen in dermatomyositis. In disseminated lupus, except as a wasting disease, I do not believe that one expects muscular atrophy. I am sure that the attention of an expert skin pathologist is required before one can be dogmatic about the diagnosis of disseminated lupus on a skin biopsy. I believe that periorbital edema is likelier to be present in dermatomyositis than in scleroderma or in disseminated lupus. I shall hazard the guess that if this were disseminated lupus over an entire year's period the patient should have had a more elevated temperature than she did have, although I should be glad to be corrected on that point. Muscular weakness is characteristic of dermatomyositis in a large number of patients and at times mimics myasthenia gravis. We know that the diagnosis of myasthenia gravis was considered because the patient was given Prostigmine as a therapeutic test. Five tenths of a milligram is the usual dose, is it not, Dr. Ayer?

DR. JAMES B. AYER: Yes.

DR. JONES: It produced no change, and it would be unusual for myasthenia gravis not to respond to such a dose. I think this diagnosis can be dismissed. Furthermore, the whole course of the disease is not too consistent with myasthenia gravis, although the patient did have progressive muscular weakness.

In considering scleroderma, there are one or two other things that I can add in a hesitating fashion. We do know that one observes gastrointestinal lesions in scleroderma, and as Hale[1] and others have shown, evidence of generalized stiffness and edema and a fibrotic condition involving the esophagus, with a lack of normal peristaltic activity. Ulcerative lesions have not been described in the gastrointestinal tract in scleroderma to the best of my knowledge. Whether dermatomyositis can be associated with similar lesions, I do not know. It is a queer disease, and I am sure that we do not know all its manifestations. Scleroderma is also a queer disease, about which we know very little. Disseminated lupus, to my knowledge, is not associated with ulcerative gastrointestinal lesions. That very fact, if I am going to stick to one diagnosis, rules out lupus, along with other things that I have mentioned.

Tuberculosis with queer skin manifestations can certainly answer this diagnostic problem. Ulcerations of the gastrointestinal tract are not too infrequent in tuberculosis and can produce, after healing, a stricture of the rectum. It is hard for me to make a single diagnosis that covers all the findings, but what I can do is to indicate the possibilities that occur to me. The terminal event, I think, was the final episode of a prolonged disease, with perforation of an ulcer and peritonitis; on the other hand, the terminal cause of death may have been a coronary accident. The linear shadows in the chest suggest pulmonary emboli, which may have occurred late in the illness. In dermatomyositis one often observes electrocardiographic changes suggesting involvement of the myocardium, as well as that of the voluntary muscles. I am not at all certain that these changes are diagnostic, but I believe they have been reported. Excessive sweating is one of the interesting phenomena supposed to take place in dermatomyositis.

That is as far as I can go without making rash statements that have no meaning whatever. I shall therefore say that this patient had gallstones and probably cholecystitis, both of which had nothing to do with the rest of the picture. I believe that she had syphilis; I am sure that such a diagnosis does not explain the whole setup, and as near as I can come to tying it in is to say that the rectal fistula might have been syphilitic in origin. Beyond that I believe that she had one of the three conditions that I have mentioned — dermatomyositis, scleroderma or disseminated lupus erythematosus. Of the three, I shall put dermatomyositis first, admitting that I know nothing about the gastrointestinal lesions in that disease. I shall choose scleroderma as a close second, because I know that digestive-tract lesions have been found on several occasions in this curious disease. It may well be that there was tuberculosis as an added factor, which would help to explain the gastrointestinal symptoms, but it had nothing to do with what originally brought her to the hospital.

I am a little intrigued by the statement, or by the fact, if it is a fact, that some of the skin lesions appeared after two doses of Mapharsen. It is possible that inadequate antisyphilitic treatment was associated with syphilitic skin lesions that can behave this way when latent syphilis is treated inadequately. I cannot explain the skin lesions on the basis of reactivation of the syphilis or on the basis of syphilis itself, except the papular lesions, which were rather odd.

I should like to see the x-ray films. I do not believe that she had tuberculosis of the stomach, which is exceedingly rare and mimics cancer.

DR. MILFORD D. SCHULZ: This is certainly a curious small-bowel pattern (Fig. 1). There is some edema of the wall. The picture is much like what Dr. Hale has described in scleroderma.[1] None of the bowel loops seem to be fixed in relation to one another for any period of time, as one would expect to see if the patient had had tuberculous peritonitis.[2]

DR. JONES: One might add that that fits in with the story that she was depleted from apparent partial intestinal obstruction. It took nine hours for barium to go through the intestinal tract, which implies that the motor activity of the small bowel was interfered with by some intrinsic nerve disorder or by an infiltrative process.

DR. SCHULZ: The fluoroscopist could have better described the findings, but the barium-filled esophagus looks wide and stiff — a lead-pipe appearance. It may have contracted later, but it had not at the moment when these films were made.

DR. JONES: Have you a picture that shows the rectal ulceration and stricture? That worried me more than anything else.

DR. SCHULZ: Here is a film after a barium enema. The ulcer seems to be in the sigmoid. The rectum appears normal. Of course there is a balloon in it, and the normal rectum does not balloon out to that size without protest.

DR. JONES: Was the balloon put in to hold the barium in the colon in order to take the picture?

DR. SCHULZ: I think that it was.

DR. JONES: In that case it suggests an atonic anal sphincter, a condition often associated with dermatomyositis or scleroderma.

DR. SCHULZ: Or syphilis.

DR. JONES: What about the linear shadows in the chest film? Do they suggest infarction?

DR. SCHULZ: Here are two that suggest scars of old infarcts; such a lesion was apparently not present on the films taken eleven months previously.

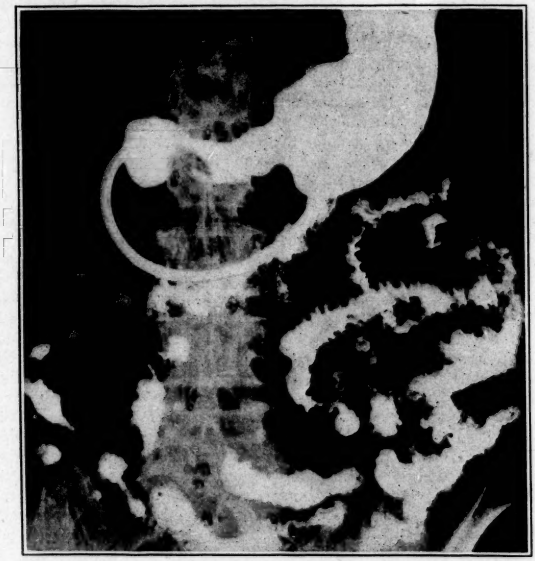

FIGURE 1. *Roentgenogram Showing the Distribution of Barium in the Small Bowel Six Hours after Administration.*
Note the evidence of slow transport and of mucosal swelling.

DR. JONES: You can see no evidence of recent infarcts?

DR. MAURICE FREMONT-SMITH: One argument for scleroderma is the tenderness over the areas of edema. I do not believe that Dr. Jones brought that out. Furthermore, an argument against lupus is the absence of albumin and red cells in the urine. I also do not know whether intestinal symptoms go with the strange disease called dermatomyositis.

DR. BENJAMIN CASTLEMAN: Dr. Lever, will you comment, from the dermatologic point of view, on the differences between these two diseases.

DR. WALTER F. LEVER: From the standpoint of the dermatologist, the diagnosis in this case lay between lupus erythematosus and dermatomyositis,

rather than between scleroderma and dermatomyositis. For a diagnosis of scleroderma, one expects a certain amount of boardlike induration of the skin and subcutaneous tissue, which was absent in this patient. The cutaneous lesions were suggestive of lupus erythematosus in that there were erythema and atrophy, but the same type of lesions can be found in dermatomyositis. In favor of dermatomyositis was the presence of tenderness over the involved areas of skin, and also the muscular tenderness. In scleroderma, muscular atrophy may be just as severe as in dermatomyositis, but usually it is not combined with tenderness of the muscles. So, from the dermatologic point of view, the diagnosis was dermatomyositis.

Clinical Diagnoses

Dermatomyositis, generalized.
Generalized peritonitis.
Acute pancreatitis?
Mesenteric thrombosis?

Dr. Jones's Diagnoses

Dermatomyositis or scleroderma.
Peritonitis, following perforation of the colon.
Old pulmonary infarcts.
Cholelithiasis.
Syphilis.

Anatomical Diagnoses

Dermatomyositis.
Ulcers of esophagus, jejunum and rectum, with perforation of several jejunal ulcers.
Fibrous and myxomatous intimal proliferation of intestinal arteries, with thromboses.
Abscess, pelvic, right.
Peritonitis, acute, fibrinopurulent.
Bronchopneumonia.
Lipid pneumonia.
Arteriosclerosis, generalized.

Pathological Discussion

Dr. Castleman: As Dr. Jones inferred, a biopsy had been done at the time of the first admission and the diagnosis of dermatomyositis was established. The autopsy also showed what Dr. Jones predicted. This woman had a perforation of the intestine, with acute purulent generalized peritonitis. Numerous sections of striated muscle throughout the body showed severe degeneration. In some areas there was no cellular infiltration, but in others it was marked. There is no question about the diagnosis of dermatomyositis.

The intestinal tract was unusual, and as could be seen from the roentgenograms of the gastrointestinal series, the small intestine, especially the jejunum, was markedly edematous. Throughout the jejunum were numerous ulcers, some tiny and others measuring up to 1 cm. in diameter. A few of these had perforated and had produced peritonitis. There were also ulcers in the rectum that were similar to those seen in the jejunum, but we did not find any evidence of stricture. There were no ulcers in the duodenum or other parts of the colon, but the entire bowel was markedly edematous, thick and brawny. Microscopic examination showed

Figure 2. *Photomicrograph of One of the Ulcers of the Small Intestine.*
Note the extensive arterial disease in the submucosa.

that most of the edema was in the submucosa. The bases of the ulcers were covered with fibrin and an extensive lymphocytic and polymorphonuclear leukocytic infiltration (Fig. 2). In the edematous

Figure 3. *Photomicrograph at a Higher Magnification of One of the Vessels in the Submucosa.*
Note the marked intimal proliferation with luminal narrowing.

submucosa beneath the ulcers, and also in regions that were not ulcerated, the large vessels showed pronounced fibrous and myxomatous intimal proliferation with marked luminal narrowing (Fig. 3). Some of the vessels were completely occluded, and

others contained recent or organized thrombi. The ulcers were almost certainly the result of the vascular disease. An occasional vessel showed organized thrombosis with recanalization (Fig. 4). These vascular lesions were found only in the intestines. We hunted throughout the sections of the various other organs but were unable to find anything similar to the lesions found in the intestine. They duplicated the changes seen by Dr. Gall in the kidneys of a case of dermatomyositis that we had several years ago.[3] In that case, the myxomatous intimal lesion was found only in the kidneys. The kidney sections in this case were perfectly normal, except for evidence of mild arteriosclerosis, certainly

FIGURE 4. *Photomicrograph of Another Vessel. Note the thrombosis with recanalization.*

nothing that simulated the vascular changes that were found in the intestines.

DR. JONES: What did you find in the heart?

DR. CASTLEMAN: Nothing. There was no degeneration. We have recently gone over all our cases of dermatomyositis and were unable to find any definite change in the heart muscle. In one case the myocardial findings were equivocal.

DR. FREMONT-SMITH: Do you call this whole disease process dermatomyositis? Is it all part of the same picture?

DR. CASTLEMAN: I believe so.

DR. MARIAN ROPES: Clinically, I have noted intestinal symptoms in at least two other cases with long periods of severe diarrhea. Such cases usually do not have guaiac-positive stools and do not reach this picture by x-ray.

DR. JONES: I should like to ask if gastrointestinal lesions have been described in dermatomyositis. That is an important point.

DR. LEVER: They have been described in a few cases. In Potain's[4] case, the autopsy revealed multiple visceral infarcts. In the case reported by Karelitz and Welt,[5] diffuse enterocolitis with intestinal ulceration was encountered. The arteries of the small intestines showed marked edema and round-cell infiltration between the fibers of the muscular layer. The case cited by Schuermann[6] presented hemorrhages into the mucosa of the stomach, with early necroses, as well as erosions in the lymphatic tissue of the lower small bowel. Vascular lesions were absent.

DR. CASTLEMAN: Because of the dermatomyositis, these patients are prone to have trouble in swallowing, as this patient had. The administration of mineral oil should be avoided, lest some of it pass down the larynx and into the lungs. This patient must have been taking mineral oil for some time, because we found a great many foci of lipid pneumonia throughout all lobes, especially the lower ones.

DR. JONES: Do you want to comment on the difference between this and scleroderma? Are the lesions of scleroderma like this?

DR. CASTLEMAN: I do not recall a case of scleroderma with bowel lesions. I have just seen a report that describes marked atrophy of the musculature of the gastrointestinal tract but no vascular lesions similar to those in this case of dermatomyositis.[7]

DR. JONES: Certainly the number of patients with scleroderma who have gastrointestinal symptoms and x-ray signs is much larger than that of those with dermatomyositis.

REFERENCES

1. Hale, C. H., and Schatzki, R. Roentgenological appearance of gastrointestinal tract in scleroderma. *Am. J. Roentgenol.* 51:407-420, 1944.
2. McCort, J. J. Roentgen features of chronic tuberculous peritonitis. *Arch. Surg.* 49:91-99, 1944.
3. Talbott, J. H., Gall, E. A., Consolazio, W. V., and Coombs, F. S. Dermatomyositis with scleroderma, calcinosis and renal endarteritis associated with focal cortical necrosis: report of case in which condition simulated Addison's disease, with comment on metabolic and pathologic studies. *Arch. Int. Med.* 63:476-496, 1939.
4. Potain. Morve chronique de forme anomale. *Bull. et mém. Soc. méd. d. hôp. de Paris* 12:314-318, 1875.
5. Karelitz, S., and Welt, S. K. Dermatomyositis. *Am. J. Dis. Child.* 43:1134-1149, 1932.
6. Schuermann, H. Zur Klinik und Pathogenese der Dermatomyositis (Polymyositis). *Arch. f. Dermat. u. Syph.* 178:414-468, 1939.
7. Bevans, M. Pathology of scleroderma, with special reference to changes in gastrointestinal tract. *Am. J. Path.* 21:25-51, 1945.

CASE 31102

PRESENTATION OF CASE

A seventy-seven-year-old widow entered the hospital because of marked dyspnea, abdominal distention and tenderness in the right upper quadrant.

Nine years before admission she had a subtotal thyroidectomy for nontoxic goiter, 140 gm. of tissue

having been removed. The pathological report was "hyperinvolution." After recovery she lived at a home for aged women, where her activities were limited. Five years before admission she received some medical attention for "gall-bladder trouble" and "a heart condition." She had at that time only shortness of breath and could not take digitalis because this caused vomiting. She spent nine weeks in bed and was well thereafter. Three months before admission she began having pain in the right upper quadrant, which came on only after lying in bed. This pain lasted up to two hours, varied in severity and had no relation to food or exertion. Long-standing constipation became accentuated and required an additional laxative tablet each day. Four days before admission she entered the Emergency Ward because of painful migratory arthritis involving both feet and the right hand. Physical examination and x-ray study at that time were consistent with rheumatoid arthritis. She was discharged to the Out Patient Department. One day before admission, distention of the abdomen began after an unsuccessful enema had been given and the patient's dyspnea increased. Repeated enemas resulted in several loose movements, without relief of the distention or the dyspnea. On the day of admission she had had two episodes of vomiting.

Physical examination revealed a dyspneic woman in moderate discomfort but without pain. The lips, ears and mucous membranes were cyanotic. The heart was not enlarged, and the sounds were normal. The neck veins were slightly distended and pulsating. Bilateral crackling basal rales were heard, and in the same areas there was increased dullness to percussion. There was no peripheral edema. The abdomen was markedly distended and tympanitic. Peristalsis was diminished. There was tenderness in the right upper quadrant. No abdominal splinting or masses were noted. Rectal examination was negative. The rectum was filled with soft, tan feces, which were guaiac negative.

The rectal temperature was 100°F., the pulse 84, and the respirations 20. The blood pressure was 168 systolic, 80 diastolic.

Examination of the blood revealed a red-cell count of 3,800,000, with 10.5 gm. of hemoglobin, and a white-cell count of 16,000, with 91 per cent neutrophils. The urine was acid and had a specific gravity of 1.016, with a ++++ test for albumin and occasional white cells and casts. The Bence-Jones protein was negative. The serum nonprotein nitrogen was 42 mg. per 100 cc., and the total protein 5.8 gm., with an albumin-globulin ratio of 1.1. The carbon dioxide and chloride levels were normal. The phosphorus was 1.4 mg. per 100 cc., and the alkaline phosphatase 10.6 Bodansky units.

X-ray films of the chest showed mottled areas of increased density scattered throughout the lungs. The vascular shadows were increased in size. The heart was prominent in the region of the left ventricle, and the aorta tortuous. Films of the abdomen showed considerable gas in the small and large bowel, neither of which appeared to be dilated. There was a laminated gallstone in the region of the gall bladder. No abnormal soft-tissue masses were seen. An electrocardiogram showed normal rhythm at a rate of 75, a PR interval of 0.16 second, a flat T_1, upright T_2 and T_3 and a diphasic T_4, with a sagging ST_4. The patient was digitalized with Cedilanid and was given sulfadiazine.

On the second hospital day the patient was considerably improved and was no longer orthopneic, dyspneic or cyanotic; the lungs had cleared but a few patches of fine rales persisted at both bases posteriorly. The abdominal distention was diminished, and two masses in the right upper quadrant could be felt 5 to 7 cm. below the costal margin. These were nontender and descended with inspiration; they were thought to be due to a coarsely irregular liver edge. The sulfadiazine level was maintained at about 10 mg. per 100 cc., with an intake of about 1250 cc. and an output of about 1000 cc.

At 12:30 a.m. on the fifth hospital day she had an episode of steady precordial pain with gradual onset. Moderately severe orthopnea, with a respiratory rate of 40, lasted about twenty minutes. Repeated electrocardiograms showed inverted T_1, T_2 and T_3 and a sagging of all ST segments. X-ray films of the chest on the same day showed that the mottled areas of increased density previously described had cleared considerably. Only moderate congestion of the vessels was noted, and no infarcts were seen in a posteroanterior view. The nocturnal dyspnea recurred during the succeeding two nights. There was no increase in the pulmonary rales.

A bromsulfalein test on the fifth hospital day, using 5 mg. of the dye per kilogram of body weight, showed 80 per cent retention in forty-five minutes. A van den Bergh test was normal. An aspiration biopsy of the liver showed no abnormality. The cephalin flocculation test was + in forty-eight hours. A barium enema was negative.

The white-cell count rose steadily and reached 31,400 on the eleventh hospital day, with 75 per cent neutrophils, 5 per cent lymphocytes, 4 per cent eosinophils and 16 per cent large monocytes. A low-grade fever (99 to 100°F.) and anemia persisted. The stools were brown and formed. The urine persisted in showing a +++ to ++++ test for albumin and a specific gravity of 1.006 to 1.020.

On the twelfth day the patient suddenly had an attack of acute pulmonary edema, for which she was treated with tourniquets, morphine, Cedilanid and, finally, venesection. She rallied but developed peripheral edema. She became incontinent, with slowly increasing depression and unresponsiveness, and died on the twenty-third hospital day.

Differential Diagnosis

Dr. Reed Harwood: Whatever else we are dealing with in this case it is evident that the patient had congestive heart failure. I think that two questions should be considered — first, the type of heart disease that was responsible for the failure and, second, whether any further disease contributed to her death.

Nine years before admission she had a subtotal thyroidectomy. This raises the question of myxedema. If she did have myxedema it is not evident from the record.

Four days before admission she came to the Emergency Ward, complaining of painful migratory arthritis. It is unusual but not impossible to see acute rheumatic fever in a person of this age; I have seen it in persons of fifty years. One would expect, however, to find an increased PR interval in the electrocardiogram and to have more statements about her joints after she was admitted to the hospital.

The low-grade fever and the anemia suggest a subacute bacterial endocarditis, but I consider that as remote. She was an old woman who had a moderate hypertension. The x-ray films showed some enlargement of the left ventricle, and I think it is likely that she had hypertensive heart disease. At her age it is reasonable to expect that she had sclerosis of the coronary arteries. I suggest that she had a combination of hypertensive and arteriosclerotic heart disease.

The initial electrocardiogram was not strikingly abnormal, and I am interested to see if the changes that took place were consistent with an infarct. She was given digitalis, and we therefore expect to find sagging of the ST segments. I cannot say with complete confidence, however, that these tracings are consistent with an infarct. But since, following the attack of precordial pain, there was a definite change in CF_4, it seems extremely likely that she had a myocardial infarct.

In answer to the first question, that is, the type of heart disease responsible for failure, I believe that she had hypertensive and arteriosclerotic heart disease, with a small myocardial infarction while she was in the hospital.

Did she have anything else that contributed to her death? She had abdominal pain and constipation shortly before admission; she was found to have a secondary anemia and a persistent ++++ test for albumin, without striking abnormalities in the urinary sediment. The attending physicians evidently considered the possibility of multiple myeloma because of the marked albuminuria and anemia, but the test for Bence-Jones protein was negative and the serum protein was not markedly increased. I do not believe that this entirely rules out multiple myeloma, but at least the evidence is against it. It was found that she had a phosphorus of 1.4 mg. per 100 cc. and an alkaline phosphatase of 10.6 Bodansky units, both of which are abnormal figures. The only condition that I know of in which the phosphorus is reduced to such a low figure is hyperparathyroidism, but that may be ignorance on my part. If at post-mortem examination an adenoma of the parathyroid gland was found, I should be willing to give the opinion now that it did not contribute to her death. I am inclined to think that she did not have an adenoma, because there is so little evidence to go with it. The alkaline phosphatase was definitely increased, which suggests some disease of the bone in which the osteoblastic activity is increased. Once again one thinks of hyperparathyroidism, Paget's disease or some type of malignant disease involving the bone.

Another finding is the presence of two masses in the right upper quadrant. For lack of a better explanation I decided that she had a liver that was probably engorged from early right-sided failure of the heart and a chronically inflamed gall bladder. Both masses were rather low in the abdomen, at least four fingerbreadths below the costal margin. She might conceivably have had a diseased kidney on that side.

We next come to the consideration of disease of the liver, about which there are many contradictory data. Evidently the attending physicians thought that she had liver disease. They did a bromsulfalein test on the day that she had acute left ventricular failure and found that she had 80 per cent retention. At the same time a van den Bergh test was normal. A biopsy of the liver was normal, and a cephalin flocculation test was not definitely abnormal. The serum protein level and the albumin-globulin ratio were normal. With all this negative evidence I am going to disregard the bromsulfalein test or at least not give it undue importance. I do not know what happens to the bromsulfalein test in cases of congestive failure, but it is at least possible that during acute congestive failure more of the dye would be retained.

Finally, there was a peculiar reaction of the bone marrow, which had produced a leukocytosis by the twelfth hospital day. I should like to know about some of the other white-cell counts and differentials during the preceding interval.

Dr. Benjamin Castleman: On admission, the white-cell count was 16,000; subsequently, it was 13,000, 18,000, 23,000 and 31,000; on the tenth day it was 32,000, and then 18,000 and 32,000. In the differential counts the neutrophils ranged from 91 to 74 per cent, and then from 71 to 77 per cent.

Dr. Harwood: When did the monocytosis appear?

Dr. Castleman: On the tenth day, there were 5 small lymphocytes and 3 monocytes; on the fifteenth day, 5 small lymphocytes, 6 large lymphocytes and 3 monocytes; three days later, 4 large lymphocytes, 9 small lymphocytes and 8 monocytes, with 2 myelocytes.

DR. WYMAN RICHARDSON: There were numerous smears interpreted by different persons.

DR. JAMES A. ROTH: The monocytes were not typical. They were large mononuclear cells, which I could not classify. They stained light blue.

DR. HARWOOD: I should like to ask Dr. Schulz if there is anything in the chest plate to suggest any disease other than congestive failure.

DR. MILFORD SCHULZ: The pulmonary markings are prominent. They do not look just like the prominent markings that are seen with lymphatic spread of a tumor. There is not much fluid in the chest. In the lateral view there is a triangular shadow in the posterior gutter that could indicate an infarct, but it is not entirely characteristic.

DR. HARWOOD: Do you want to say anything about the bones?

DR. SCHULZ: All the bones are decalcified but no more than one would expect in a person of her age. There is no evidence of cysts, and no change in the vertebral bodies. There are old arthritic changes in the hands and feet. I do not see any localized areas of destruction.

DR. HARWOOD: Is there anything suggestive of miliary tuberculosis in the lungs?

DR. SCHULZ: The picture is not consistent with that of miliary tuberculosis. Lungs that look like this are disturbing. One thinks of passive congestion, early lymphatic spread of malignant disease, pulmonary fibrosis and even miliary tuberculosis; something similar is often seen in diseases like periarteritis nodosa.

DR. HARWOOD: Do you see anything in the lungs that suggests the need for sulfadiazine? The temperature was 100°F. when the patient came in, and she had a high white-cell count. There is nothing in the record, however, to give me a clue why sulfadiazine was necessary, and this raises the question why patients have to be treated with some kind of chemical. We know that occasionally a fever subsides without their use, and I doubt that this patient needed sulfadiazine. I shall proceed, leaving the statement for what it is worth.

To go on with the discussion, I think that some other disease besides heart disease was found post mortem. I have no idea what, but the evidence points to a lesion that involved bone. I should think, first of all, of a malignant tumor with widespread metastasis, including involvement of the lungs. The original site of such a tumor I cannot determine. It may have been the thyroid gland, the gall bladder or some other intra-abdominal organ.

Another possibility is miliary tuberculosis. The evidence for this is not striking. I also thought of the possibility of some acute intra-abdominal catastrophe to explain the increasingly high white-cell counts, such as thrombosis or embolus of some vessel or perhaps perforation of the gall bladder. I remember a patient with carcinoma of the prostate who developed a high fever and chills. I thought that he had a kidney infection, but at post-mortem examination we found that the gall bladder had ruptured into the bed of the liver, discharging a hundred or more small stones. It was an entirely unsuspected finding. In the present case, I also thought of the possibility of disease in the liver. The likeliest lesion would be a metastatic carcinoma.

DR. RICHARDSON: I did not see this patient, but I did see a blood smear taken at about the midpoint of her illness. At that time she had received sulfadiazine for some time. The picture was that of a considerable degree of leukocytosis. There was no evidence of infection from the smear. There were some peculiar cells, which might have been very immature red cells, and I thought that the whole picture might have been due to sulfonamide therapy. Sulfonamides had been stopped, however, a few days previously, but still the total white-cell count remained elevated. There was also red-cell regeneration. I wrote in my note that since the picture had continued after the stopping of sulfonamides it was quite consistent with involvement of the bone marrow, presumably by a malignant tumor that had also produced considerable anemia. There were no toxic changes such as are usually seen in uremia, nor was it hypochromic by measurement. It was a "simple anemia" but must be explained somehow.

Not knowing the answer in this case, I should say that the patient probably had malignant involvement of the bone marrow. The possibility of myeloma should be considered. Those queer cells might conceivably have been immature plasma cells.

DR. CHESTER M. JONES: I should like to take minor exception to one statement that Dr. Harwood made, namely, that an elevated phosphatase means disease of bone. That is not correct because an elevation of the phosphatase level may also occur in liver disease and may be as high or higher than that noted in involvement of bone.

DR. HARWOOD: Is that true in patients without jaundice?

DR. JONES: Yes.

Dr. Harwood was entirely right in stating that the elevation of the bromsulfalein retention could be explained by congestive failure. No doubt one could observe dye retention, positive cephalin flocculation and Takata Ara tests and at least some change in the albumin-globulin ratio as a temporary episode occurring with congestive failure. On the other hand, 80 per cent retention in forty-five minutes is extremely high.

I do not recall this case too well, since the patient came in at a time when I was out of the hospital for a few days. I do recall, however, that we entertained the thought of metastatic cancer of the liver as a real possibility and that is why the biopsy was

done. The fact that nothing was found on aspiration biopsy is no proof against its existence. One can miss a nodule very easily.

Clinical Diagnosis

Metastatic carcinoma to lungs and liver?

Dr. Harwood's Diagnoses

Hypertensive and arteriosclerotic heart disease, with congestive failure.
Carcinoma of gall bladder or thyroid gland, with metastases to bone marrow?

Anatomical Diagnoses

Carcinoma of gall bladder, with extension into liver and with metastases to lung, liver, peritoneum and bone marrow.
Cardiac hypertrophy, hypertensive type, slight.
Cholelithiasis.
Hydrothorax, slight, bilateral.

Pathological Discussion

Dr. Castleman: The post-mortem examination disclosed a heart weighing over 400 gm., with slight hypertrophy of the left ventricular wall, which is consistent with a mild hypertensive heart. There was no infarction, and the coronary arteries were only slightly sclerotic. We found no real evidence of heart failure. There was about 50 cc. of fluid in both pleural cavities. The liver showed no evidence of chronic passive congestion, but it was enlarged. In the region of the gall bladder was a mass about 6 or 8 cm. in diameter that completely replaced the gall bladder and that looked like carcinoma. It extended into the liver substance for about 4 or 5 cm. In cutting through this mass we found a gallstone embedded within. Microscopic sections revealed that this was a primary carcinoma of the gall bladder. The increase in pulmonary markings was due to metastatic carcinoma.

Dr. Richardson: What about the bone marrow?

Dr. Castleman: There were also metastases to the peritoneum and to the bone marrow.

Dr. Schulz: Was the entire bone marrow replaced?

Dr. Castleman: We have not seen enough sections to say, but the one section that I examined certainly showed extensive involvement.

Dr. Jones: This woman was given sulfonamides with the idea that she had a bacterial pneumonia.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. John Fallon, M.D.

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board
Joseph Garland, M.D. Charles C. Lund, M.D.
Shields Warren, M.D. A. Warren Stearns, M.D.
C. Guy Lane, M.D. Dwight O'Hara, M.D.
William A. Rogers, M.D. Chester S. Keefer, M.D.
Stephen Rushmore, M.D. Fletcher H. Colby, M.D.
Henry R. Viets, M.D. Robert L. Goodale, M.D.
Robert M. Green, M.D. Chester M. Jones, M.D.
Harvey R. Morrison, M.D.

Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

"KEEP 'EM ALIVE IN 'FORTY-FIVE"

It has been well said that instead of trying to make ourselves happier and other people better, we should make ourselves better and other people happier. The American Red Cross, which is now conducting its annual War Fund drive, is making a great many people happier — or at least much less miserable. In so far as the Nation supports its endeavors, we shall be a better people. Immediate incentives are the mounting casualty and prisoner-of-war lists, and the enthusiastic endorsement of the Red Cross by military and naval leaders.

The number of chapters in Greater Boston — twenty-two — amalgamated for the drive is the highest yet; they represent thirty-nine communities in the Metropolitan Area. Under the general chairmanship of Kenneth H. Erskine, each chapter will have its own War Fund chairman and treasurer, with committees for special gifts, business contributions and house-to-house solicitation. General campaign headquarters have been opened at 101 Milk Street, with volunteer organizations set up on three floors.

The necessity for the Red Cross is too obvious and widely known to require emphasis. General Eisenhower has said of the organization, "We simply couldn't get along without it." The Red Cross budget for 1945 represents an increase of 12.5 per cent over the previous year, so that it behooves all who can contribute to the drive to do so, and to the most generous extent possible.

THE "PSYCHONEUROTIC"

Sometime sportswriter Bill Cunningham has acquired new stature as he has found new fields in which to try his strength. In the January 21 issue of the *Boston Herald* he took his fling at the stubbornly cherished belief that a diagnosis of psychoneurosis, particularly when it has been applied to a soldier, constitutes a stigma denoting mental deterioration or moral weakness.

Grave injustices are being done to many thousands of innocent and capable young men who are being prejudiced in their opportunities to re-enter industry and normal civilian life, and it is at least partly the job of the country's doctors to educate the public to a better understanding of the profession's more commonly used terminology. To the lay mind, apparently, any word containing the root "psycho" (from the Greek, meaning soul; derived from the word Psyche — a lovely maiden with wings like a butterfly) implies organic disease of the soul or mind, in other words, insanity — and there seems to be no doubt in Greek mythology that Cupid was crazy about Psyche.

The shell shock of World War I, which was an induced psychoneurosis, was considered to have been brought about by physical forces and consequently was an illness that respectable soldiers could have. The same forces, acting on the mind

by more subtle agencies than violent ethereal disturbances, place their victim in the ranks of the untouchables, distrusted by industry and frequently held in contempt by friends and family. The polite term "battle fatigue," which has been offered as a substitute for the quasi-scientific psychoneurosis, suggests the warrior worn out in the defense of his country — hence, an acceptable hero, worthy of sympathy and help.

A literal-minded medical corps apparently did not realize the trouble that could be caused by the unguarded classification of disease. Either it underrated the velocity, impact and explosive force of the "psycho" root, or it overestimated the intellectual capacity of the general public on the home front. At any rate, the damage was done, and our hats are off to Bill Cunningham for his discerning effort to undo it.

In the February 1 issue of the *Journal*, Lieutenant Colonel Jackson M. Thomas emphasized the distinction between genuine psychoneurotics and many of these soldiers whose emotional stability has cracked after a greater or less exposure to the enormous psychic trauma of combat conditions. The genuine psychoneurotic, a victim of hidden conflicts, is a person otherwise normal who cannot face certain situations of everyday environment. The soldier with a simple adult maladjustment is a normal person who has passed his limit of reacting normally to abnormal environmental conditions. It must be recognized, moreover, that soldiers thus wounded are often among the finest and bravest that an army produces. The best thing that can be done for them is to treat them like the other sick and wounded, not classifying and grouping them with the psychotic.

In closing, it does not seem inappropriate to point out that many of the actions of the average man savor of the psychoneurotic; that some of our most brilliant generals occasionally exhibit lack of self-control; that one of the greatest leaders of the Civil War was forced to give up his command for several months, being sorely beset by doubts; that not only genius but even courage may follow various paths, not all of them obvious to everyone. The breaking point of any substance is determined not entirely by its own resistance but also by the type as well as the degree of force applied to it.

MASSACHUSETTS MEDICAL SOCIETY

APPLICANTS FOR FELLOWSHIP

PUBLISHED IN ACCORDANCE WITH THE PROVISIONS OF THE BY-LAWS (CHAPTER V, SECTION 2) AS AMENDED MAY 26, 1942

BARNSTABLE DISTRICT

HOWES, HERMON E., South Chatham.
Boston University School of Medicine, 1943.

KUNTZ, HARRIETTE H., Dennis.
Northwestern University Medical School, 1939.

JULIUS G. KELLEY, *Secretary*
Barnstable County Sanatorium, Pocasset

BRISTOL NORTH DISTRICT

McCAFFREY, JEROME A., Cross and Elm Streets, Norton.
Middlesex University School of Medicine, 1934. Sponsor: Frederick V. Murphy, 79 Bank Street, Attleboro.

WILLIAM J. MORSE, *Secretary*
34 Sanford Street, Attleboro

BRISTOL SOUTH DISTRICT

GORMAN, JOHN J., 595 Harvard Street, Fall River.
College of Physicians and Surgeons of Baltimore, 1908.

LOUD, NORMAN W., 423 Eldridge Street, Fall River.
Harvard Medical School, 1919.

QUINN, JAMES M., 74 Rockland Street, New Bedford.
Georgetown University School of Medicine, 1943.

WILSON, JAMES C., Edgartown.
University of Vermont College of Medicine, 1904.

ALBERT H. STERNS, *Secretary*
31 Seventh Street, New Bedford

ESSEX NORTH DISTRICT

ARAKELIAN, MICHAEL J., 100 Haverhill Street, Methuen.
Kansas City University of Physicians and Surgeons, 1932. Sponsor: Francis A. O'Reilly, 349 Haverhill Street, Lawrence.

CHART, STANLEY G., 1 William Street, Shawsheen, Andover.
Middlesex University School of Medicine, 1934. Sponsor: Abraham Ash, 281 Haverhill St., Lawrence.

EIDAM, CARL L., 88 East Haverhill Street, Lawrence.
Royal College of Physicians and Surgeons, Edinburgh, 1937. Sponsor: Harold R. Kurth, 57 Jackson Street, Lawrence.

FISCHER-GALATI, THEODORE I. M., 104 Main Street, Andover.
University of Vienna, 1909. Sponsor: Harry V. Byrne, 301 Essex Street, Lawrence.

GESING, EMIL J., 197 Prospect Street, Lawrence.
Kansas City University of Physicians and Surgeons, 1932. Sponsor: Francis A. Cregg, 506 Prospect Street, Methuen.

SCARITO, NINA E., 9 Houston Avenue, Methuen.
Woman's Medical College of Pennsylvania, 1941.

SHANNON, MARTIN J., JR., 63 Allston Street, Lawrence.
Tufts College Medical School, 1943.

HAROLD R. KURTH, *Secretary*
57 Jackson Street, Lawrence

ESSEX SOUTH DISTRICT

LOGLER, FRANK J., 15 Ives Street, Beverly.
Vanderbilt University School of Medicine, 1937.

NUSSBAUM, JULIUS, 291 Summer Street, Lynn.
University of Vienna, 1925. Sponsor: Saul M. Marcus, 27 Nahant Street, Lynn.

HENRY D. STEBBINS, *Secretary*
26 Chestnut Street, Salem

Hampden District

Cordero, Gil J., 52 High Street, Springfield.
Missouri College of Medicine and Science, 1927. Sponsor: Charles L. Furcolo, 14 Maple Street, Springfield.

Edelman, Waldo G. A., 684 Main Street, Agawam.
College of Physicians and Surgeons, Boston, 1935. Sponsor: William A. R. Chapin, 121 Chestnut Street, Springfield.

Halton Edward J., 1456 Northampton Street, Holyoke.
Jefferson Medical College, 1938.

Joffe, Ellis, 231 Chestnut Street, Holyoke.
Brussels University School of Medicine, 1933. Sponsor: Patrick E. Gear, 188 Chestnut Street, Holyoke.

Jorczak, John S., 250 School Street, Chicopee.
College of Physicians and Surgeons, Boston, 1931. Sponsor: Harry L. Roberts, 6 Temple Street, Springfield.

Klar, Jacob J., 1020 Sumner Avenue, Springfield.
College of Physicians and Surgeons, Boston, 1935. Sponsor: H. Bernard Tillman, 115 State Street, Springfield.

Monyek, Milton S., 3 Colony Road, West Springfield.
Middlesex University School of Medicine, 1939. Sponsor: Jacob I. Weisman, 34 Maple Street, Springfield.

Posner, Sigmund J., 1 Elm Street, Ludlow.
College of Physicians and Surgeons, Boston, 1938. Sponsor: William A. R. Chapin, 121 Chestnut Street, Springfield.

Visconti, James J., 630 Westfield Street, West Springfield.
Mid-West Medical College, 1935. Sponsor: Arthur H. Riordan, 147 Oak Street, Indian Orchard.

George C. Steele, *Secretary*
39 Upper Church Street, West Springfield

Middlesex East District

Atwood, Eldridge D., 36 Pleasant Street, Woburn.
College of Physicians and Surgeons, Boston, 1926. Sponsor: Daniel L. Joyce, 269 Main Street, Woburn.

Roy W. Layton, *Secretary*
8 Porter Street, Melrose

Middlesex South District

Avery, Jean C., 60 Prospect Street, Framingham.
Boston University School of Medicine, 1943.

Beckman, William W., 6 Craigie Circle, Cambridge.
Harvard Medical School, 1935.

Bird, Kenneth T., 775 Trapelo Road, Waltham.
Harvard Medical School, 1943.

Bushueff, Boris P., 775 Trapelo Road, Waltham.
Harvard Medical School, 1943.

Cotton, Bert H., 90 Clarke Street, Newton Centre.
University of Oklahoma School of Medicine, 1937.

Cyr, Donat P., 403 Parker Street, Newton Centre.
Georgetown University School of Medicine, 1938.

Grice, David S., 108 Holden Green, Cambridge.
University of Rochester School of Medicine, 1938.

Kateman, A. Eugene, 1706 Commonwealth Avenue, Brighton.
Middlesex University School of Medicine, 1938. Sponsor: S. Seymour Horlick, 1860 Commonwealth Avenue, Brighton.

Leavitt, Joseph S., 318 Clifton Street, Malden.
University of Lausanne Faculty of Medicine, 1936. Sponsor: Harry L. McDonald, 414 Pleasant Street, Malden.

Lynch, William A., 1522 Washington Street, West Newton.
Tufts College Medical School, 1942.

Osborne, Joseph, 139 Morton Street, Newton Centre.
Boston University School of Medicine, 1941.

Perry, Mary E., 11 Chetwynd Road, West Somerville.
Tufts College Medical School, 1940.

Wanning, Patricia E., 9 Shady Hill Square, Cambridge.
Yale University School of Medicine, 1940.

Alexander A. Levi, *Secretary*
481 Beacon Street, Boston

Norfolk District

Boehme, Earl J., 235 Woodland Road, Chestnut Hill.
University of Minnesota Medical School, 1934.

Branca, Alfred W., 86 Greenbrier Street, Dorchester.
Tufts College Medical School, 1943.

Glickman, Abraham J., 11 Wilcock Street, Dorchester.
University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1904. Sponsor: Myer I. Berman, 1071 Blue Hill Avenue, Dorchester.

Kagan, Samuel, 1405 Beacon Street, Brookline.
Mid-West Medical College, 1935. Sponsor: Arthur Berk, 270 Commonwealth Avenue, Boston.

Karpati, Oscar, 3 Brewster Terrace, Brookline.
Royal Hungarian "Elizabeth" University of Pecs, 1926. Sponsor: Isaac R. Jankelson, 483 Beacon Street, Boston.

LeCompte, Philip M., 103 Longwood Avenue, Brookline.
Yale University School of Medicine, 1936.

Orlov, Morton, 28 Waumbeck Street, Roxbury.
Tufts College Medical School, 1943.

Phillips, Joseph H., 245 Pond Avenue, Brookline.
Harvard Medical School, 1939.

Pratt, Edward L., 6 Autumn Street, Boston.
Harvard Medical School, 1940.

Robbins, Albert I., 68 Hutchings Street, Roxbury.
University of Vermont College of Medicine, 1939.

Sagall, Elliot L., 116 Riverway, Boston.
Harvard Medical School, 1943.

Shuman, Samuel B., 304 Washington Street, Dorchester.
Middlesex University School of Medicine, 1937. Sponsor: Harry Korb, 512 Blue Hill Avenue, Roxbury.

Thompson, Kenneth W., 29 Church Street, Dedham.
Harvard Medical School, 1929.

Wright, Richard H., 698 River Street, Mattapan.
Tufts Medical School, 1943.

Zeltzerman, Israel, Station Hospital, Presque Isle Air Base, Presque Isle, Maine (present temporary address).
Tufts College Medical School, 1936.

Zeltzerman, Morris, Pondville Hospital, Walpole.
Tufts College Medical School, 1933.

Charles J. E. Kickham, *Secretary*
1101 Beacon Street, Brookline

Plymouth District

Creeden, Francis V., 327 Boylston Street, Brockton.
Georgetown University School of Medicine, 1941.

Del Colliano, Michael R., Washington Street, South Easton.
Middlesex University School of Medicine, 1936. Sponsor: George A. Moore, 167 Newbury Street, Brockton.

Shapiro, Harry, 64 Seaver Street, Stoughton.
Middlesex University School of Medicine, 1931. Sponsor: Jacob Brenner, 8 Oliver Street, North Easton.

Ralph C. McLeod, *Secretary*
Goddard Hospital, Brockton

Suffolk District

Alexander, Walter J., 137 Peterboro Street, Boston.
University of Buffalo School of Medicine, 1942.

Bloomfield, Richard A., Boston City Hospital, Boston.
Harvard Medical School, 1938.

Duston, Charles H., U. S. Marine Hospital, Cleveland, Ohio.
Tufts College Medical School, 1938.

Forziati, Anthony A., 35 Washington Avenue, Winthrop.
Middlesex University School of Medicine, 1932. Sponsor: George H. Schwartz, 19 Princeton Street, East Boston.

Greenfield, Harold B., 14 Coral Avenue, Winthrop.
College of Physicians and Surgeons, Boston, 1937. Sponsor: Jacob J. Abrams, 562 Shirley Street, Winthrop.

Mailey, Howard D., 133 Peterboro Street, Boston.
Boston University School of Medicine, 1942.

NEYLAN, MARGUERITE M., 20 Ash Street, Boston.
New York Medical College, 1942.

SMITH, M. FRANCES H., 239 Commonwealth Avenue, Boston.
Boston University School of Medicine, 1943.

ROBERT L. GOODALE, *Secretary*
330 Dartmouth Street, Boston

WORCESTER DISTRICT

KARP, LEWIS S., 460 Park Avenue, Worcester.
Middlesex University School of Medicine, 1937. Sponsor: Joseph W. O'Connor, 36 Pleasant Street, Worcester.

KRESSLER, AUGUSTA H., 11 Lee Street, Worcester.
Woman's Medical College of Pennsylvania, 1941.

McKENNA, HAROLD J., U. S. Veterans Facility, Rutland Heights.
Creighton University School of Medicine, 1927.

LESLIE P. LELAND, *Secretary*
57 Cedar Street, Worcester

WORCESTER NORTH DISTRICT

COLBY, FRED B., 4 Ashburnham Street, Fitchburg.
University of Lausanne, 1937. Sponsor: Rudolf F. Bachmann, 910 Main Street, Fitchburg.

GROSSMAN, MYER J., 352 Crescent Street, Athol.
Middlesex University School of Medicine, 1933. Sponsor: Francis X. Dufault, 245 School Street, Athol.

SILVER, JOSEPH M., 24 Prichard Street, Fitchburg.
Middlesex University School of Medicine, 1933. Sponsor: Bartholomew P. Sweeney, 5 Gardner Place, Leominster.

WESTLIN, RICHARD V., 936 Main Street, North Leominster.
Imperial Alexanders University in Helsingfors, Finland, 1907. Sponsor: Edward A. Adams, 44 Oliver Street, Fitchburg.

EDWARD A. ADAMS, *Secretary*
44 Oliver Street, Fitchburg

NOTICES

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Tuesday, March 13, at 8:15 p.m.

PROGRAM

Clinical case presentation from the Massachusetts General Hospital.

Studies on Pleuropneumonia-Like Organisms in Human Beings. Drs. L. Dienes, W. E. Smith, J. V. Meigs, C. L. Parsons, and M. W. Ropes.

The Circulatory Action of Protoveratrine. Dr. O. Krayer.

Studies with Venous Catheterization. Drs. L. Dexter, C. S. Burwell, F. W. Haynes, and R. E. Seibel.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, March 14. The case presentations will be held in the Ether Dome, Bulfinch Building, Massachusetts General Hospital, and all other events at Longwood Towers, Brookline.

PROGRAM

4:00–5:30 Case Presentations: Pediatrics and Surgery by the Children's Medical Service, Massachusetts General Hospital.
6:30 Refreshments.
7:00 Dinner.
8:00 Annual meeting.
8:30 Newer Concepts in the Management of the Newborn. Dr. Stewart H. Clifford.

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club of Boston on Friday, March 16. There will be an x-ray conference at 4:30 p.m. At 8:00 p.m., the following program will be presented:

The Rectum and Sigmoid: New methods of roentgenologic examination. Dr. George Levene.

The Rectum and Sigmoid: Surgical management of inflammatory and malignant lesions. Dr. Richard B. Cattell.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, March 21, at 8 p.m. Mr. Kurt S. Lion will speak on the topic, "The Physics of Short-Wave Therapy."

A council meeting will be held at 6:00 p.m., followed by an informal dinner in the Empire Room at 6:30 p.m.

Members of the medical profession are cordially invited.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 15

FRIDAY, MARCH 16

*9:00–10:00 a.m. Proteolytic Enzymes in Tissues. Dr. Paul C. Zamecnik. Joseph H. Pratt Diagnostic Hospital.

*9:00–10:00 a.m. Medical Clinic. Isolation Amphitheater, Children's Hospital.

10:50 a.m. Bacterial Infections of the Skin. Dr. G. Schwartz. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Mallory Building, Boston City Hospital.

SATURDAY, MARCH 17

*10:00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, MARCH 19

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, MARCH 20

*9:00–10:00 a.m. Medical Clinic. Infants' Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, MARCH 21

*9:00–10:00 a.m. The Diagnosis of Diabetes Mellitus. Dr. Joseph Rosenthal. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

MARCH 13. Harvard Medical Society. Notice elsewhere on this page.

MARCH 14. New England Pediatric Society. Notice elsewhere on this page.

MARCH 16. New England Roentgen Ray Society. Notice elsewhere on this page.

MARCH 21. New England Society of Physical Medicine. Notice elsewhere on this page.

APRIL 12. Progress in Dermatology as a Result of World War II. Dr. John G. Downing. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

APRIL 30. New York Institute of Clinical Oral Pathology.

MAY 22-24. Hotel Statler, Boston. Annual meeting of the Massachusetts Medical Society.

JUNE 14-19. American Board of Obstetrics and Gynecology.

SEPTEMBER 17. American Public Health Association. Page 752, issue of November 30.

DISTRICT MEDICAL SOCIETIES

PLYMOUTH

MARCH 15. Goddard Hospital, Brockton.
APRIL 26. Toll House, Whitman.
MAY 17. Lakeville Sanatorium, Lakeville.
All meetings will be held at 11 a.m.

WORCESTER

MARCH 14. Worcester Memorial Hospital.
APRIL 11. Hahnemann Hospital, Worcester.
MAY 9. Annual meeting.